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INTRAMUSCULAR PRESSURE

IN

VASCULAR DISEASE AND COMPARTMENT SYNDROMES

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INTRAMUSCULAR PRESSURE IN VASCULAR DISEASE AND COMPARTMENT SYNDROMES

Abstract

A standardized procedure for measurement of intramuscular (intracompartmental) pressure with the wick technique was developed. Reference values for intramuscular pressure at rest, and during and after exercise were obtained. An increased intramuscular pressure was found in patients with DVT, venous claudication, intermittent claudication, lymphedema and following femoral and popliteal arterial revascularization procedures as well as in chronic compartment syndromes. The leg swelling in venous claudication, DVT including phlegmasia cerulea dolens, lymphedema and following arterial revascularization procedures was correlated to the elevation of intramuscular pressure. An increased intramuscular pressure resulted in an increased deposition of platelets onto femoral artery vascular grafts in an animal experimental model of a compartment syndrome. The development of a compartment syndrome as the cause of early graft failure following distal revascularization procedures is probably underestimated. A chronic compartment syndrome was found in 14 % of patients with lower leg pain of unknown cause.

Analysis of muscle biopsies revealed that the increased intramuscular pressure can be explained by an increased muscle water content. An increased intramuscular pressure during exercise resulted in a decreased muscle blood flow and increased muscle lactate concentrations.

Intramuscular pressure measurement is important in the evaluation of iliofemoral thrombosis with phlegmasia cerulea dolens, venous claudication, distal revascularization procedures and the chronic compartment syndrome. Fasciotomy is often indicated in iliofemoral thrombosis with phlegmasia cerulea dolens, in distal revascularization procedures and always in acute and chronic compartment syndromes.

Key words
Intramuscular pressure, wick catheter, DVT, phlegmasia cerulea dolens, venous claudication, intermittent claudication, lymphedema, femoral revascularization, popliteal revascularization, compartment syndromes, muscle blood flow, muscle metabolism, fasciotomy.

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INTRAMUSCULAR PRESSURE
IN
VASCULAR DISEASE AND COMPARTMENT SYNDROMES

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VASCULAR DISEASE AND COMPARTMENT SYNDROMES

by

Peter Qvarfordt

Lund 1983

The present thesis is based on the following papers, which will be referred to in the text by their Roman numerals.

I. Reference values for intramuscular pressure in the lower leg in man.
Peter Qvarfordt, Bo Eklöf and Per Ohlin.
Clin Physiol 2:427-434, 1982.

II. Intramuscular pressure in the lower leg in deep vein thrombosis and phlegmasia cerulea dolens.
Peter Qvarfordt, Bo Eklöf and Per Ohlin.
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III. Intramuscular pressure, blood flow and skeletal muscle metabolism in patients with venous claudication.
Peter Qvarfordt, Bo Eklöf, Per Ohlin, Gunnar Plate and Bengt Saltin.
Surgery, accepted for publication.

IV. Intramuscular pressure in the claudicant leg.
Peter Qvarfordt, Jan T. Christenson, Bo Eklöf and Per Ohlin.
VASA, accepted for publication.

V. Intramuscular pressure after revascularization of the popliteal artery in severe ischemia.
Peter Qvarfordt, Jan T. Christenson, Bo Eklöf and Per Ohlin.
Br J Surg, accepted for publication.

VI. Intramuscular pressure changes during and after revascularization of the femoral arteries in man.
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VII. The influence of increased intramuscular pressure on platelet adhesion in PTFE-grafts in vivo. An experimental model.
Jan T. Christenson, Peter Qvarfordt, Sven-Erik Strand, D Arvidsson, Trygve Sjöberg, Per-Ingvar Olsson.
Submitted to Thromb Haemost.

VIII. Intramuscular pressure, venous function and muscle blood flow in patients with lymphedema of the leg.
Peter Qvarfordt, Jan T. Christenson, Bo Eklöf, Per-Ebbe Jönsson and Per Ohlin.
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IX. Intramuscular pressure, muscle blood flow and skeletal muscle metabolism in the chronic anterior tibial compartment syndrome.
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1. INTRODUCTION

1.1. Intramuscular pressure and intramuscular pressure measurement

Microcirculation in muscle tissue is influenced by four pressures: capillary blood pressure, capillary blood oncotic pressure, tissue fluid oncotic pressure and tissue (interstitial) fluid pressure. Tissue fluid pressure in skeletal muscle enclosed by fascia, a muscle compartment, is called intramuscular or intracompartmental pressure. Tissue fluid pressure was first measured in subcutis by a needle technique (Landerer 1884). Measurements of intramuscular pressure were first applied by French & Price (1962) and later by Reneman (1968) and Whitesides et al (1975). They used a needle-water manometer system requiring injection of saline into the muscle. Matsen et al (1976) used a variant of the needle technique that employs continuous infusion of saline. The wick catheter technique, first developed by Scholander (1968) was modified for clinical use by Mubarak et al (1976, 1978 b). It was designed to prevent blockage of the catheter's tip and to maximize contact between saline in the catheter and the tissue fluid. Continuous recordings also during exercise are possible with this method. Wick catheters are also used to collect small volumes of tissue fluid for studies of transcapillary fluid exchange (Fadnes & Aukland 1977). The slit catheter, developed by Rorabeck et al (1980) is a modification of the wick catheter.

There are only a few studies of normal intramuscular pressures in man. The normal resting pressure in the anterior tibial compartment and in the flexor muscles of the forearm was 4 ± 4 mm Hg with the wick technique (Mubarak et al 1976).

1.2. Increased intramuscular pressure and compartment syndromes

A compartment syndrome is a condition in which increased pressure within a compartment compromises the circulation to the tissues within that space (Matsen 1975). Symptoms of a compartment syndrome are pain and tenseness over the affected compartment, pain with passive stretch of the muscles within the compartment and sensory deficit. Paresis may be a late symptom. Except in the presence of arterial injury or arteriosclerotic arterial disease peripheral pulses are usually normal. Compartment syndromes are divided into two forms, acute and chronic (see Mubarak & Hargens 1981). An acute compartment syndrome is a severe form which untreated is irreversible and leads to tissue necrosis. A wide variety of injuries may initiate a compartment syndrome. The most common cause of an acute compartment syndrome is fracture (45 %), the majority being fractures of the tibia. Soft tissue injury and arterial injury with postischemic swelling are also common causes. Most of these cases have occurred in the leg (see Mubarak & Hargens 1981). The chronic compartment syndrome represents a recurrent form. It was first described by Mavor (1956). Since then more than 100 cases have been described. Reneman (1975) reported the largest series of chronic compartment syndromes, 61 cases, all

involving the anterior tibial compartment. Most cases were young male military personnel and the symptoms were bilateral in 95 %. Symptoms of the chronic compartment syndrome are exertion pain similar to but more long-lasting than that of intermittent claudication although there is no sign of arterial disease. Neurologic symptoms are rare. A fascial defect with muscle hernia is the most specific physical sign of the chronic anterior tibial compartment syndrome (Reneman 1975). The chronic compartment syndrome takes an intermittent course. It does not generally lead to necrosis within the affected compartments (Reneman 1975), although transition to an acute compartment syndrome has been reported (Leach et al 1967). The intramuscular pressure is always abnormally raised (French & Price 1962, Kenelly & Blumberg 1968, Reneman 1975, Puranen & Alavaikko 1981). The pathophysiology of the chronic compartment syndrome is not known. It is provoked by exercise and it has also been named exertional compartment syndrome. It has been suggested that arterial (Griffiths 1940, Kinmonth 1952, Freedman & Knowles 1959) or venous (Leach et al 1967, Paton 1968, Barcia 1972) obstruction are initiating factors. A common concept is that the raised intramuscular pressure inducing closing of capillaries is caused by an increase in interstitial fluid (Hargens et al 1978, Matsen et al 1979). The increased volume of interstitial fluid may be secondary to a marked hyperosmolarity (Lundvall 1972, Rorabeck & Macnab 1975, Hargens et al 1978 b). The anterior tibial compartment is most commonly affected probably due to its strong fascial covering. Chronic compartment syndromes involving the superficial posterior compartment (gastrocnemius and soleus muscles) are rare (Kirbu 1970, Mubarak et al 1978 a). There are only few thorough studies of patients with chronic anterior tibial compartment syndrome (French & Price 1962, Kenelly & Blumberg 1968, Reneman 1975). The diagnosis has often been made without intramuscular pressure measurement documentation.

Intramuscular pressure is elevated either by compartment volume constriction (external compression, tight casts, burn echars) or by an increased compartment content (hemorrhage, muscle hypertrophy, increased interstitial fluid volume). Intracompartmental edema may result from venous and lymphatic obstruction and an increased capillary permeability due to ischemic endothelial damage in arteriosclerotic occlusive disease and following peripheral arterial reconstructive surgery. Experimental studies have shown that venous occlusion due to the massive intravenous thrombosis in phlegmasia cerulea dolens causes an increased intramuscular pressure (Brockman & Vasko 1966, Snyder 1967). This disorder has been successfully treated by fasciotomy in a few cases (Dennis 1945, Cywes & Louw 1962). Venous claudication is seen clinically in patients with chronic iliac vein obstruction (Cockett & Lea Thomas 1965, 1967, Bjordal 1970, Møller et al 1980, Tripolitis et al 1980). So far, no studies on intramuscular pressure in patients with venous disease have been reported. Fluid return via lymphatic vessels is important for removing excess extracellular fluid in muscle and lymphatic obstruction causes edema of the leg (Kinmonth 1982). Despite this fact no studies on intramuscular pressure in lymphedema are available. Whitesides et al (1971) studied

intramuscular pressure following tourniquet ischemia in the dog hind limb. Intracompartmental pressure rose upon tourniquet release. The magnitude of the pressure rise corresponded directly with the duration of tourniquet application. Extensive edema was produced after ischemia for 8-10 hours. There is only one study on intramuscular pressure in leg ischemia in man. Thus, an elevated intramuscular pressure was found in patients with intermittent claudication after exercise (Reneman & Jageneau 1973). Massive swelling of the lower extremity is frequently seen after peripheral vascular procedures (Husni 1967, Vaughan et al 1970, Porter et al 1972, Patman 1975, Eickhoff & Engell 1982). The mechanism of this swelling is not fully understood. Postischemic increased capillary permeability (Whitesides 1971, Patman 1975), old postthrombotic changes with venous hypertension and post-operative acute deep vein thrombosis may be factors responsible for the edema after arterial reconstruction (Husni 1967, Barcia et al 1972, Filippone et al 1980). Some authors have suspected the surgical trauma to the lymphatic vessels being the main factor responsible for the edema (Vaughan et al 1970, Porter et al 1972, Eickhoff & Engell 1982). The postischemic swelling may initiate a compartment syndrome leading to early graft failure (Mubarak & Hargens 1981). The importance of relieving fasciotomy in these cases has been stressed by Patman (1970). In his review of 2 000 peripheral arterial reconstructive procedures the frequency of fasciotomy was, however, only 0.45 %. There are no previous studies of intramuscular pressure in the lower extremity following reconstructive peripheral vascular surgery in man. The effects of increased intramuscular pressure on vascular graft blood flow and graft patency have not been studied before.

Many investigators have demonstrated that increased intramuscular pressure reduces blood flow in experimental models (Zelis et al 1974, Ashton 1975, Rorabeck & Macnab 1975, Rorabeck & Clarke 1978, Matsen et al 1979). An increased intramuscular pressure has been shown to decrease capillary blood flow (Hargens et al 1978, Reneman et al 1980) which may cause ischemia and necrosis of the tissues within the compartment. Recent studies of capillary blood pressure (Hargens et al 1977, 1978) and capillary blood flow (Reneman et al 1980) indicate that muscle microcirculation is compromized at intramuscular pressures as low as 30 mm Hg. The time period of increased intramuscular pressure is an important factor for the development of tissue necrosis (Rorabeck & Clarke 1978). Thus, an increased pressure at 30 mm Hg for 6-8 hours has been shown to cause irreversible tissue damage (Hargens et al 1981). Apart from the studies of French & Price (1962), Kenelly & Blumberg (1968) and Clayton et al (1977) the relation between intramuscular pressure and muscle blood flow has not previously been investigated in clinical conditions. Although there is general agreement (Patman & Thompson 1970, Reneman 1975, Rorabeck & Macnab 1975, Hargens et al 1977, Matsen et al 1979) that fluid accumulation within a compartment leading to tissue ischemia is the common denominator for most compartment syndromes there are no studies on muscle water content and skeletal muscle metabolism in patients with elevated intramuscular pressure.

Since the common denominator for all compartment syndromes is elevated intramuscular pressure, surgical decompression of the affected compartments seems to be the treatment of choice. Fasciotomy to prevent Volkmann's contracture in the forearm was first reported by Bardenheuer (1911). Fasciotomy in the treatment of an acute compartment syndrome in the leg was first reported by Sirbu et al (1944). DeBakey and Simeone (1946) described fasciotomy in the treatment of arterial injuries in World War II. Chronic compartment syndromes were successfully treated with fasciotomy by Mavor (1956) and Reneman (1975).

2. AIMS OF THE PRESENT INVESTIGATION

During the last two decades acute compartment syndromes secondary to trauma have been extensively documented (see Bradley 1973, Sheridan & Matsen 1976, Mubarak & Hargens 1981). There are, however, only rudimentary studies of intramuscular pressure in patients with peripheral arterial, venous and lymphatic disease or following peripheral reconstructive vascular surgery. A chronic anterior tibial compartment syndrome has previously been studied thoroughly only in a few reports. The effects of increased intramuscular pressure on blood flow and tissue metabolism have not been investigated in detail in clinical conditions. The present investigation was therefore performed:

1. To obtain reference values for intramuscular pressures at rest and during and after exercise using the wick technique (I).

2. To estimate alterations in intramuscular pressures following venous and arterial occlusion in healthy individuals (I).

3. To estimate intramuscular pressure in deep vein thrombosis including phlegmasia cerulea dolens in order to see whether there is a correlation between intramuscular pressure and the severity of clinical and phlebographic findings (II).

4. To determine intramuscular pressure in patients with chronic iliac vein obstruction and venous claudication (III).

5. To determine intramuscular pressure in patients with intermittent claudication (IV).

6. To determine intramuscular pressure and the degree of leg swelling before and after revascularization of the popliteal (V) and femoral (VI) arteries in severe ischemia.

7. To study the effect of clamping and declamping of the aorta on intramuscular pressure in reconstructive surgery for arteriosclerotic disease of the aortic bifurcation (VI).

8. To study the effect of increased intramuscular pressure on arterial blood flow and platelet-vascular graft-surface interaction in an animal experimental model (VII).

9. To determine intramuscular pressure in patients with lymphedema of the leg (VIII).

10. To demonstrate the intramuscular pressure changes that are diagnostic of a chronic anterior tibial compartment syndrome (IX).

11. To study the effect of increased intramuscular pressure on muscle blood flow (III, VIII, IX) and muscle metabolism (III, IX) in humans.

12. To study muscle water content in patients with increased intramuscular pressure (III, IX).

13. To evaluate the need for fasciotomy in the treatment of deep vein thrombosis, venous claudication, intermittent claudication, after peripheral vascular reconstructive surgery and chronic compartment syndromes (II, III, IV, V, VI, VIII, IX).

14. To determine the effect of fasciotomy on symptoms, intramuscular pressure, muscle blood flow and skeletal muscle metabolism in patients with a chronic compartment syndrome (IX).

3. METHODS

3.1. Intramuscular pressure measurement (I-IX)

The wick catheter technique was used to measure intramuscular pressure. In the wick catheter fibrils protrude from the bore of the catheter to prevent an obstruction of the catheter tip. The wick catheter was introduced through a 16 gauge epidural needle into the muscle compartment under local anesthesia. Thereafter the epidural needle was removed leaving the wick catheter in place. The pressures were recorded with an electromagnetic transducer and recorder (Siemens-Elema, Sweden). The zero level was taken at the level of the tip of the catheters. The catheters were filled with sterile heparinized saline.

3.2. Muscle blood flow measurement (III, VIII, IX)

Muscle blood flow was measured in the anterior tibial or gastrocnemius muscles using the ^{133}Xenon clearance technique. Approximately 3.5 MBq ^{133}Xenon in 0.1 ml of isotonic saline was injected into the muscle about 15 cm below the knee joint at a depth of about 2 cm using a needle with 0.4 mm outer diameter. The isotope was slowly injected during 15 sec and the needle was withdrawn 15 sec later. Records were taken from both legs with the patient at rest, and during and 5 min after exercise. The number of pulses were recorded directly over the site of injection with a collimated cadmium telluride detector (TE 101, Pharmacia Electronics, Denmark) attached to the skin surface of the legs with adhesive tape. The detector was connected to a portable memory, Memolog-500 (Pharmacia Electronics, Denmark) working as a multiscaler giving digital information of the number of pulses in 8 sec intervals which after each study was written directly into a computer (ABC 80, Luxor, Sweden). The blood flow (f) was calculated from the half-time ($T_{\frac{1}{2}}$) of the disappearance of the isotope according to the following formula:

$$f = \frac{\ln 2 \cdot \lambda \cdot 60 \cdot 100}{T_{\frac{1}{2}}}$$

where λ represents the partition coefficient for ^{133}Xenon between tissue and blood. A standardized value of 0.7 µl/g was used for λ, since it has been used previously for muscle tissue (Lassen et al 1964). The calculated muscle blood flow is expressed as ml x min^{-1} x (100 g)$^{-1}$ tissue.

3.3. Metabolic analysis (III, IX)

Muscle biopsies were extracted with a Radner forceps (No 13717, AB Stille Werner, Sweden) from the anterior tibial or the gastrocnemius muscle about 15 cm beneath the knee joint under local anesthesia. The biopsies were taken from both legs at rest and immediately after a

maximal work load. The muscle specimens were immediately frozen in isopentane cooled to freezing point and stored at -80°C until analysis. ATP, phosphocreatine (CP) and lactate were analyzed using enzymatic fluorometric techniques (Saltin et al 1981 b). Total muscle water was obtained by weighing the samples before and after freeze drying.

3.4. Venous (VIII, IX) and arterial function (III, IV, V, VI, VIII, IX)

Venous emptying was performed according to Hallböök et al (1970). A tourniquet applied around the thigh was pumped up to 50 mm Hg. The calf volume was registered with strain-gauge technique. When no further increase of calf volume was noted the tourniquet was released and the venous outflow measured. Values below 40 ml x min^{-1} x (100 g)$^{-1}$ tissue were regarded as subnormal (Hallböök et al 1970). Systolic pressure of the big toe was measured with strain-gauge technique and a standardized walking test on the tread mill (speed 1.2 m x sec^{-1}, inclination 5 %) was carried out to evaluate arterial disease.

3.5. Fasciotomy (IX)

Fasciotomy was performed in either local or general anesthesia. Following an anterolateral skin incision 5-10 cm in length, the anterior tibial and the lateral compartments were decompressed from the fibular head to the lateral malleolus using a Smilley knife.

3.6. Experimental model of a compartment syndrome (VII)

In anesthetized pigs with PTFE grafts in the femoral circulation (both superficial femoral arteries) an increased intramuscular pressure of 30 mm Hg or more was achieved in one hind limb by means of a blood pressure cuff. The contralateral hind limb served as control. Intramuscular pressure was measured with the wick technique bilaterally in the anterior compartment of the lower hind limb. Blood flow in the femoral arteries was continuously measured with non-cannulating electromagnetic square wave flowmeters (Nycotron, Sweden). The effect of increased intramuscular pressure on the deposition of platelets on vascular graft surface was studied by employment of ^{111}Indium-labeled autologous platelets and scintillation camera - scintigraphy.

4. THE PRESENT INVESTIGATION

4.1. Intramuscular pressure in health (I)

Reference values for intramuscular pressure at rest and during and after exercise were studied in healthy individuals of both sexes at different ages. The alterations in intramuscular pressures following venous and arterial occlusion were also estimated since arterial and venous disease is known to influence intramusuclar pressures.

Procedure. Intramuscular pressures in the anterior tibial and superficial posterior compartments of the leg were measured by the wick technique in 34 healthy individuals. The leg was kept horizontally with the subject in a sitting position and the foot attached to an isometric exerciser, continuously monitoring the workload to verify that the work was constant during the exercise.

Results. The intramuscular pressure was found to be below 23 mm Hg in the anterior tibial compartment and below 15 mm Hg in the superficial posterior compartment at rest. The intramuscular pressure at rest decreased with increasing age. During exercise the intramuscular pressure increased markedly. At exercise the anterior tibial compartment pressure was lower in females than in males. After exercise the pressures were back to the pre-exercise levels within 5 min. Venous occlusion caused an increase in the pressure which was more marked in the anterior tibial compartment than in the superficial posterior compartment. Arterial occlusion for 3 min did not cause any dramatic changes in intramuscular pressures, but there was a slight elevation during the period of reactive hyperemia.

Conclusion and clinical implication. The wick catheter technique was found to be a convenient method for measuring intramuscular pressure. Reference values for intramuscular pressure was obtained for the anterior tibial and the superficial posterior compartments at rest and during and after exercise. These reference values are useful for the evaluation of acute and chronic compartment syndromes.

4.2. Intramuscular pressure in venous disease (II, III)

4.2.1. Deep vein thrombosis and phlegmasia cerulea dolens (II)

Intramuscular pressure was estimated in deep vein thrombosis including phlegmasia cerulea dolens to see whether there is a correlation between intramuscular pressure and the severity of clinical and phlebographic findings.

Procedure. Twenty-two patients with DVT were studied. The diagnosis was established by phlebography. Intramuscular pressure was measured in the anterior tibial and the deep posterior compartments in both legs in the supine patient at rest and during a few seconds of passive tension of the calf muscles (Homans' maneuver). The healthy leg served

as a control. The pressures were measured before treatment and then daily for four days. Patients were treated with heparin and an antiprothrombinolytic drug. In eight patients (including three patients with phlegmasia cerulea dolens) with an iliofemoral thrombosis a venous thrombectomy and a temporary AV-fistula for six weeks to prevent rethrombosis was carried out.

Results. The intramuscular pressure was significantly ($p < 0.001$) higher in the thrombosed leg than in the contralateral leg (0-16 mm Hg). Iliofemoral thrombosis caused a significantly ($p < 0.001$) higher pressure (17-28 mm Hg) than calf thrombosis (16-23 mm Hg). In iliofemoral thrombosis with phlegmasia cerulea dolens the pressure was 47-56 mm Hg at rest. One patient with phlegmasia cerulea dolens developed gangrene. During Homans' maneuver intramuscular pressure in the deep posterior compartment increased more in the thrombosed leg than in the control leg.

Conclusion and clinical implication. Intramuscular pressure is increased in DVT. The increment of the intramuscular pressure in the lower leg is dependent on the extension of the thrombus. Thus, there is a very marked increase of the intramuscular pressure in iliofemoral thrombosis with phlegmasia cerulea dolens causing a compartment syndrome. In these cases intramuscular pressure measurements are suggested to evaluate the need for fasciotomy.

4.2.2. Venous claudication (III)

The present study was designed to determine intramuscular pressure in patients with venous claudication due to chronic iliac vein obstruction and to assess the effects on muscle blood flow and skeletal muscle metabolism.

Procedure. Nine patients with unilateral venous claudication were studied. Intramuscular pressure was measured in the anterior tibial and the deep posterior compartments in both legs at rest and during exercice (heel-raising) provoking venous claudication. Leg muscle blood flow was studied with ^{133}Xenon clearance technique and muscle metabolism and water contents of biopsies from the gastrocnemius muscles were studied before and immediately after exercise.

Results. The intramuscular pressures in the deep posterior compartment were significantly higher in the leg with iliac vein obstruction, 39 ± 10 mm Hg, than in the contralateral leg, 26 ± 12 mm Hg at rest as well as during exercise, 60 ± 16 mm Hg and 41 ± 15 mm Hg, respectively. Similar observations were made for the anterior tibial compartment. The results regarding muscle blood flow and skeletal muscle metabolism are given on page 20 and in III.

Conclusion and clinical implication. The intramuscular pressure is increased in patients with chronic iliac vein obstruction. Therefore, fasciotomy might be of value in the treatment of venous claudication.

Studies need to be done to evaluate fasciotomy as a therapeutical procedure in patients with venous claudication.

4.3. Intramuscular pressure in arterial disease (IV, V, VI)

4.3.1. Intermittent claudication (IV)

Intramuscular pressures were determined in patients with intermittent claudication at rest and during and after pain-provoking exercise.

Procedure. Intramuscular pressure in the anterior tibial and the superficial posterior compartments was determined in 10 patients with intermittent claudication at rest and during and after exercise. The pressure results in claudicants were compared with matched intramuscular pressure reference values in 10 healthy subjects.

Results. Intramuscular pressures did not differ significantly between the two groups at rest. During exercise the intramuscular pressures were significantly ($p < 0.001$) higher in the claudicant group in both the anterior tibial, 30 ± 6 mm Hg and the superficial posterior compartment, 14 ± 3 mm Hg, than in the healthy subjects, 24 ± 5 mm Hg and 7 ± 2 mm Hg, respectively.

Conclusion and clinical implication. The elevated intramuscular pressure seen in patients with intermittent claudication during exercise may contribute to impair tissue blood perfusion and aggravate ischemic pain. It may be supposed that fasciotomy may be of benefit in the treatment of intermittent claudication.

4.3.2. Following revascularization of the femoral and popliteal arteries (V, VI)

In the present study intramuscular pressure and the degree of leg swelling were determined before and after revascularization of the popliteal arteries in severe ischemia and the need of fasciotomy in these cases was evaluated. Furthermore, the effect on intramuscular pressure of clamping and declamping of the aorta and femoral revascularization in reconstructive surgery for arteriosclerotic disease of the aortic bifurcation was studied.

Procedure. Fourteen patients undergoing revascularization of the popliteal artery and five patients undergoing revascularization of the femoral arteries by bifurcation grafting because of occlusive arteriosclerotic disease were studied by intramuscular pressure and calf circumference measurements on the day before operation and once every day during 5-8 days postoperatively. In the femoral revascularization group intramuscular pressure was measured before and after clamping and immediately and 4-6 hours after declamping.

Results. In the popliteal revascularization group calf circumference increased to a maximum swelling of 3.9 ± 1.1 cm on the sixth

postoperative day. There was a gradual increase in intramuscular pressure from 9 ± 2 mm Hg on the day before operation in the anterior tibial compartment to a maximum pressure on the sixth to seventh postoperative day, 26 ± 4 mm Hg. Similar intramuscular pressure changes were seen in the superficial posterior compartment. A postoperative compartment syndrome with graft failure was observed in one case. In the patients undergoing revascularization of the femoral arteries by bifurcation grafting intramuscular pressure increased to a maximum 4-6 hours after re-establishing blood flow, 22 ± 5 mm Hg, followed by a gradual decrease over five postoperative days. Changes in calf circumferences reflected the changes in intramuscular pressure. During occlusion of the aorta (clamping) no changes in intramuscular pressure were seen, but the pressure increased significantly immediately after declamping.

Conclusion and clinical implication. Revascularization of the popliteal artery causes swelling of the lower leg and an increased intramuscular pressure which may lead to a compartment syndrome and perhaps graft failure within about one week. Therefore, follow-up of intramuscular pressure in patients with marked swelling after distal revascularization procedures is recommended and early fasciotomy may be considered on wide indications. The risk for development of compartment syndromes after clamping of the aorta and femoral revascularization seems minimal.

4.4. Intramuscular pressure in lymphedema of the leg (VIII)

The present study was undertaken in order to evaluate the effect of leg edema of lymphatic origin on intramuscular pressure, venous function and muscle blood flow.

Procedure. Seven patients with unilateral lymphedema of the leg were studied. The lymphedema was secondary to extirpation of lymph nodes and radiation therapy in the treatment of malignant melanoma in six patients. One patient had essential lymphedema. The leg swelling was considerable with an increase in calf circumference of 5.2 ± 1.5 cm in the sick leg as compared to the contralateral leg. The patients had moderate pain in the leg on heavy exercise. Intramuscular pressure measurement was performed as described previously for patients with venous claudication (III). Venous emptying, distal blood pressure and muscle blood flow were also estimated in these patients.

Results. The intramuscular pressures in the anterior tibial compartment were significantly ($p < 0.01$) higher in the diseased than in the healthy leg both at rest (30 ± 14 mm Hg and 16 ± 8 mm Hg, respectively) and during exercise (49 ± 16 mm Hg and 28 ± 6 mm Hg, respectively). Similar pressure differences were found in the deep posterior compartment. Venous emptying was significantly lower ($p < 0.05$) in the diseased leg than in the healthy leg. In two edematous legs venous emptying was markedly below the normal value. No arterial disease was found. The results of muscle blood flow are given on page

20 and in VIII.

Conclusion and clinical implication. Lymphatic obstruction of the leg causes edema which leads to an increased intramuscular pressure and a decreased maximal rate of venous emptying.

4.5. Intramuscular pressure in the chronic anterior tibial compartment syndrome (IX)

The present study was made in order to 1) demonstrate the intramuscular pressure changes that are diagnostic of a chronic anterior tibial compartment syndrome, 2) evaluate the relationship between muscle blood flow and intramuscular pressure, 3) study the metabolism in the anterior tibial muscles before fasciotomy, 4) test previous arterial and venous occlusion theories in the pathogenesis of this syndrome by determining distal blood pressure and venous emptying and 5) determine the effect of fasciotomy on intramuscular pressure, muscle blood flow and skeletal muscle metabolism.

Procedure. One hundred and eight non-selected patients with lower leg pain of unknown cause were referred for intramuscular pressure measurement during a three-year period. In 93 patients the intramuscular pressures in the anterior tibial compartment were within normal limits both at rest and during and after exercise when compared with a reference material (I). In 15 patients or about 14 % (seven females and eight males, aged 17-50, mean 29 years) the pressures were significantly increased both at rest and during exercise and a bilateral chronic anterior tibial compartment syndrome was diagnosed. These 15 patients were further investigated. Distal blood pressure and venous emptying were measured. Muscle blood flow was determined in the anterior tibial muscles at rest and during exercise. Biopsies were taken from the anterior tibial muscles before exercise and immediately after exercise for determination of water content and muscle metabolism.

Fasciotomy was performed and all patients were re-investigated three months after fasciotomy.

Results. Intramuscular pressure was 22 (range 18-28) mm Hg at rest rising to 80 (range 48-135) mm Hg during exercise. These pressure values are significantly ($p < 0.001$) higher than the corresponding reference values (I). The return to resting values after exercise took 10 min to 2 hours (mean 40 min). Systolic pressure of the big toe was normal in all patients. Venous emptying was normal in the majority of cases. When studied three months after fasciotomy 14 patients were symptom-free while one patient still had moderate symptoms. The pressures were normalized. Furthermore, after exercise the pressure was back to the resting level within 1 min. The results of muscle blood flow and skeletal muscle metabolism are given on page 20 and in IX.

Conclusion and clinical implication. This study shows, that 14 % of patients with exertional pain in the lower leg not due to arteriosclerotic occlusive disease suffer from a chronic anterior tibial compartment syndrome. This diagnosis can only be made by means of intramuscular pressure measurement during and after exercise. Fasciotomy cures over 90 % of the patients. Arterial and venous disease are not the underlying etiologic factors.

4.6. Increased intramuscular pressure and muscle blood flow (III, VIII, IX) and skeletal muscle metabolism (III, IX)

The present investigations illustrate the effect of increased intramuscular pressure on muscle blood flow as well as the effect of increased intramuscular pressure and decreased muscle blood flow on skeletal muscle metabolism. Furthermore, muscle water content was estimated in patients with increased intramuscular pressure.

Procedure. Muscle blood flow was studied at rest and during pain-provoking exercise in a total of 22 patients with abnormally increased intramuscular pressure (chronic anterior tibial compartment syndrome, n = 10; venous claudication, n = 5; leg lymphedema, n = 7). Skeletal muscle metabolism and muscle water content was studied in 11 patients with abnormally increased intramuscular pressure both at rest and immediately after exercise (chronic anterior tibial compartment syndrome, n = 6; venous claudication, n = 5). Muscle blood flow was measured using the ^{133}Xenon clearance technique in the anterior tibial compartment (VIII, IX) and in the superficial posterior compartment (III). Muscle biopsies were taken from the anterior tibial muscles (IX) and the gastrocnemius muscles (III) for the metabolic studies.

Results. Muscle water content was elevated in legs with increased intramuscular pressure. Muscle blood flow was lower in compartments with increased pressure than in control legs during exercise. Muscle lactate increased with exercise in both legs but the elevation was larger ($p < 0.05$) in the affected leg. The exercise caused ATP and CP to become reduced in both the control and the affected legs. In the chronic anterior tibial compartment syndrome fasciotomy tended to normalize the abnormal changes in muscle blood flow, lactate concentration and muscle water content.

Conclusion and clinical implication. Increased intramuscular pressure may be explained by the increased muscle water content. The increased intramuscular pressure causes a decreased muscle blood flow with an increased lactate concentration during exercise. Fasciotomy relieves pain, normalizes intramuscular pressure and reverses changes in muscle blood flow, skeletal muscle metabolism and water content.

4.7. Increased intramuscular pressure and vascular graft patency (VII)

The effects of increased intramuscular pressure on arterial vascular graft blood flow and platelet deposition on the graft surface were

studied in pigs.

Procedure. Six pigs were anesthetized and both femoral arteries were exposed. PTFE (polytetrafluoroethylene) grafts (Gore-Tex®) 4 mm internal diameter, 5 cm long, were implanted in the femoral circulation (superficial femoral artery) using end-to-end anastomoses with interrupted 6-0 Prolene sutures. Intramuscular pressure was measured bilaterally in the anterior compartment of the lower limb using the wick technique. Platelets were labeled with ^{111}Indium and reinfused intravenously. Blood flow in both superficial femoral arteries were measured. The ^{111}Indium activity was recorded by a scintillation-camera and platelet deposition onto the graft was calculated. The platelet uptake was recorded after re-establishing blood flow through the grafts and after increased intramuscular pressure (external compression) on one side.

Results. Vascular graft blood flow decreased by 12 % of the initial blood flow when intramuscular pressure was increased 30 mm Hg and by 20 % when it was increased to 60 mm Hg. When the intramuscular pressure was increased platelet deposition onto the graft increased.

Conclusion and clinical implication. The present experimental study in pigs showed that an increased intramuscular pressure in the hind limb leads to a decreased blood flow in a femoral graft and an increased deposition of platelets onto vascular graft surface. These factors predispose for graft failure. The fact that distal revascularization procedures frequently cause a considerable elevation of intramuscular pressure (V) stresses the need for intramuscular pressure follow-up after peripheral vascular surgery and for early fasciotomy.

5. DISCUSSION

5.1. Methodological considerations

5.1.1. Intramuscular pressure measurement

The measurement of intramuscular (intracompartmental) pressure is the most objective and reliable parameter for the diagnosis of acute and chronic compartment syndromes. Therefore, a good technique for pressure measurement is essential. The principal advantage of the wick catheter (Mubarak et al 1976) over needle techniques (Reneman 1968, 1975, Whitesides et al 1975, Matsen et al 1976, Brooker & Pezeshki 1979) is that no injection or continuous infusion of saline which might increase pressure, is necessary. Furthermore, continuous monitoring of pressure even during muscle contractions was possible with this method. Blockage of the catheter's tip seldom occurred, probably because of the large contact area with the tissue fluid that the fibres at the end of the wick catheter constitute. There were no complications, neither infection, nor major bleeding, in more than 1 000 recordings with the wick catheter in the present 209 patients and volunteers.

5.1.2. Muscle blood flow measurement

The ^{133}Xenon technique has been widely used for determination of muscle blood flow. ^{133}Xenon is considered to be freely diffusible in the tissue and the blood-tissue diffusion equilibrium is therefore efficient and rapid, even at high blood flow rates (Lassen et al 1965, Tönnesen & Sejrsen 1967). The ^{133}Xenon technique shows a high correlation between degree of exercise and blood flow and it agrees quantitatively with perfusion experiments in animals and plethysmography in humans (Tönnesen 1964). Therefore, it seemed natural to use the ^{133}Xenon technique in the present investigation. Several investigators have found an inverse relationship between tissue pressure and blood flow as measured with ^{133}Xenon (Clayton et al 1967, Dahn et al 1967, Rorabeck & Clarke 1978).

5.1.3. Experimental model of a compartment syndrome

In the present animal model in pigs an increased intramuscular pressure was obtained by using a blood pressure cuff around the calf. The method of applying external pressure on the extremity to elevate tissue pressure, creating a compartment syndrome has been described previously (Matsen et al 1977). Other experimental methods to create compartment syndromes are inflation of latex balloons within compartments (Sheridan & Matsen 1975), blood (Rorabeck & Clarke 1978) or plasma (Hargens et al 1978) infusion and applying tourniquet ischemia (Whitesides et al 1971) to achieve postischemic swelling and elevated pressure. Venous obstruction (Jepson 1926) has also been used to create compartment syndromes. We found that limb compression was the most convenient method to create a well-defined increase in

intramusuclar pressure in the hind limb of the pig.

5.2. Increased intramuscular pressure in vascular disease and compartment syndromes

A fluid accumulation in a compartment is considered to be an important factor for the development of a compartment syndrome (see Mubarak & Hargens 1981). The fluid accumulation could be either extracellular or intracellular. Intracellular edema is known to occur during post-ischemic swelling (Reneman 1968, Patman & Thompson 1970, Whitesides et al 1971, Mubarak & Owen 1975). Extracellular edema is produced by several factors such as increased capillary permeability, elevated capillary blood pressure (Reneman 1968, Patman & Thompson 1970) or lymphatic obstruction (Kinmonth 1982). The present finding of an increased water content in muscle biopsies in patients with increased intramuscular pressures (III, IX) agrees with the concept that fluid accumulation is important for the increased pressure.

Venous occlusion gives an increased capillary blood pressure which causes an augmented transudation resulting in an increased amount of extracellular fluid (Brockman & Vasko 1966, Zelis et al 1974). As a matter of fact compartment syndromes can be produced experimentally by means of venous occlusion (Jepson 1926). In the present study this was true for iliofemoral thrombosis with phlegmasia cerulea dolens. Also less wide-spread deep venous thromboses were found to cause increased intramuscular pressure (II).

Lymphatic occlusion leads to an increased tissue concentration of protein giving an increased colloid osmotic pressure in the tissue and resulting in an increased interstitial fluid content (Kinmonth 1982). This correlates with the present finding of an increased intramuscular pressure in lymphedema (VIII). It has been suggested that venous and lymphatic systems co-operate to reduce accumulation of tissue fluid in the following way: if venous occlusion occurs the lymphatic flow increases and vice versa (Pflug & Calnan 1973). From the present findings it seems obvious, however, that one of the two systems is not sufficient to maintain a normal intramuscular pressure.

In arterial disease with intermittent claudication the normal trans-capillary movement of fluid known to occur during exercise may be enhanced leading to an increase of interstitial fluid (Reneman et al 1973). The mechanism behind the increased transudation is supposed to be an ischemic damage to the capillary walls (Reneman et al 1973). This increase in extracellular fluid might well explain the present findings of an increased intramuscular pressure during exercise. Contrary to Reneman (1973) no augmented intramuscular pressure was found after exercise. Another explanation of increased intramuscular pressure in these patients may be swelling of the muscle fibres due to increased lactate formation (Lundvall 1972).

Postischemic increased capillary permeability (Whitesides et al 1971, Patman 1975) is probably the main factor behind the leg swelling and the increased intramuscular pressure seen after peripheral revascularization procedures. The present finding of a dramatically increased intramuscular pressure during the first week after popliteal revascularization (V) emphasizes the importance of this mechanism. Intramuscular pressure was nearly unaffected by short-term ischemia during femoral occlusion but there followed a light elevation during the period of reactive hyperemia (I). After cross-clamping of the aorta there was a significant increase of pressure during six hours after declamping of the aorta (VI). This corresponds to the reversible fibre edema seen after incomplete temporary muscle ischemia (Sjöström et al 1982).

In the chronic anterior tibial compartment syndrome the elevated intramuscular pressure is thought to be due to an increased transudation of fluid during exercise (Reneman 1975, Rorabeck & Macnab 1975, Hargens et al 1978). The intramuscular pressure might remain elevated after exercise until the interstitial fluid volume becomes normal again (Reneman 1975). The present finding that the pressure return - time was as a mean 40 min indicates that the normalization of muscle water content after exercise is a slow process in these patients. The increased pressure in chronic compartment syndromes at rest may be due to muscle hypertrophy (Wright 1961). Therefore, it seems likely that in a chronic compartment syndrome intracellular as well as extracellular fluid is increased. Another proposed mechanism for the chronic compartment syndrome is that exercise leads to hemorrhage from torn muscle fibres which should increase interstitial fluid (see Mubarak & Hargens 1981). The increased intramuscular pressure may lead to a vicious cycle with ischemia resulting in an augmented capillary permeability with a further increase in interstitial fluid. The normal pressure rise during a muscle contraction is probably due to tissue compression and a decreased venous blood flow from the muscle (Reneman 1975).

5.3. Increased intramuscular pressure and muscle blood flow

Many investigators (French & Price 1962, Dahn et al 1967, Kenelly & Blumberg 1968, Zelis et al 1974, Ashton 1975, Rorabeck & Macnab 1975, Clayton et al 1977, Rorabek & Clarke 1978, Matsen et al 1979) have demonstrated in animal experiments that increased intramuscular pressure reduces muscle blood flow. Muscle blood flow has been measured in man at increased external pressures (Dahn et al 1967) but there is little information on muscle blood flow in clinical conditions with elevated intramuscular pressures. French & Price (1962) and Kenelly & Blumberg (1968) found a significantly reduced muscle blood flow as demonstrated by clearance of ^{22}Na-chloride following exercise in four patients with a chronic anterior tibial compartment syndrome. Clayton et al (1977) compared compartment pressures as determined by the open needle technique with ^{133}Xenon determinations of muscle blood flow in an animal model and in patients

with suspected compartment syndromes. There was a high degree of correlation between increasing intramuscular pressure and decreasing muscle blood flow. A decreased muscle blood flow shown by the clearance of ^{133}Xenon was also found during exercise in the present investigation in patients with elevated intramuscular pressures (III) and compartment syndromes (IX).

Increased intramuscular pressure might reduce muscle blood flow either as a result of active closure of small arterioles by a high tone in the vasomotor nerves when the transmural pressure is lowered or by passive collapse of the capillaries when tissue pressure rises above intracapillary pressure (Ashton 1975). Hargens et al (1977, 1978, 1981) have postulated that capillary perfusion is reduced at an intramuscular pressure of 30 mm Hg. The modern concept favours passive collapse of capillaries as the reason for decreased blood flow when intramuscular pressure is increased. Thus, Reneman (1980) demonstrated, using vital microscopy in an experimental model of a compartment syndrome, that muscle capillary blood flow stopped in the presence of dilated arterioles and venules. The mechanism involved in the cessation of muscle blood flow at the capillary level is, however, incompletely understood and needs further investigation (Reneman 1980).

5.4. Increased intramuscular pressure and skeletal muscle metabolism

Remarkably few studies have been carried out investigating skeletal muscle metabolism in patients with increased intramuscular pressure. Increased intramuscular pressure has been shown to reduce muscle oxygen tension (Sheridan et al 1977, Nicholas & Miller 1978, Matsen et al 1979). The present findings indicate that increased intramuscular pressure in venous claudication and in the chronic anterior tibial compartment syndrome has marked effects on skeletal metabolism as noted as an increased lactate concentration.

5.5. Clinical considerations

In the present investigation an increased intramuscular pressure was found in chronic iliac vein obstruction with venous claudication, deep vein thrombosis including phlegmasia cerulea dolens, intermittent claudication, lymphedema and the chronic compartment syndrome. Furthermore, intramuscular pressure was elevated following femoral and popliteal arterial revascularization procedures. The swelling of the leg seen in venous claudication, deep vein thrombosis including phlegmasia cerulea dolens, lymphedema and following arterial revascularization procedures is correlated to the elevation of intramuscular pressure. In cases with DVT the increment of intramuscular pressure was correlated to the extension of the thrombus. Markedly increased intramuscular pressures well above 30 mm Hg were found in iliofemoral thrombosis causing phlegmasia cerulea dolens. This means that a compartment syndrome in the lower leg is a part of the entity phlegmasia cerulea dolens. The increase in intramuscular pressure was

large enough to decrease muscle blood flow in patients with venous claudication due to chronic iliac vein obstruction, lymphedema and a chronic compartment syndrome.

Pain is one of the classic signs in phlegmasia cerulea dolens, venous and intermittent claudication and in chronic compartment syndromes. The pain is very likely due to the increased intramuscular pressure that leads to ischemia. Mubarak et al (1978 b) reported that pain appears when the intramuscular pressure reaches approximately 30 mm Hg. In the present study it was noted that passive dorsiflexion of the foot (Homans' maneuver) inducing a marked short-lasting increase in the intramuscular pressure caused pain in patients with deep vein thrombosis. This finding may indicate that pain in connection with high intramuscular pressure is not only due to ischemia. It seems reasonable to assume that the pressure increase also might activate pain receptors. The pain in venous claudication is possibly caused by the increased intramuscular pressure and it seems unlikely that the relative ischemia or the accumulation of lactate is responsible for the pain. The possibility that pain is produced by nociceptor stimulation of the distended vein wall has been been discussed (Cockett et al 1967). It should be noted that Negus (1968) did not find any evidence that venous distension or muscle ischemia caused the pain in venous claudication. In patients with intermittent claudication the pain is undoubtedly ischemic in its origin. In this context it must be pointed out, however, that the cause of the ischemic pain is unknown (Saltin 1981 a).

In patients with arteriosclerotic occlusive disease the distal blood pressure is reduced. Therefore, the tissue blood perfusion will be inadequate even with a relatively mild increase in intramuscular pressure (Reneman et al 1973). Thus, the increased intramuscular pressure seen in patients with intermittent claudication during exercise as compared with healthy subjects may contribute to decrease tissue blood perfusion and perhaps aggravate pain.

Postoperative leg swelling due to postischemic increased capillary permeability following popliteal revascularization is well known to all vascular surgeons. Deep vein thrombosis in the postoperative course (Barcia et al 1972) and interruptions of lymphatic channels (Vaughan et al 1970, Porter et al 1972, Eickhoff & Engell 1982) may contribute to the swelling. The present investigation shows for the first time that the leg swelling is accompanied by a marked increase in intramuscular pressure. The increase in intramuscular pressure might induce a compartment syndrome, which should be deleterious to the graft patency. A postoperative compartment syndrome with graft failure was actually seen in the present series (V). Increased intramuscular pressure may thus predispose for early graft failure which was also indicated by the present in vivo investigation using a pig model (VII). When intramuscular pressure was increased platelet deposition onto the graft increased. Obviously, an increased platelet deposition in the graft leads to a narrowing of the graft lumen

resulting in a decreased blood flow which predisposes for graft thrombosis. Graft thrombosis is common following distal reconstructions with small diameter grafts (Darling & Linton 1972, Hallet et al 1981, Weisel et al 1981). The risk for the development of a compartment syndrome as the cause of early graft failure following distal revascularization procedures is probably underestimated. The leg swelling and increased intramuscular pressure following femoral revascularization is less pronounced and less durable with a maximum already on the operating day following declamping. The risk for the development of a compartment syndrome in these cases seems minimal.

The chronic anterior tibial compartment syndrome may be more common than reflected in the literature (see Mubarak & Hargens 1981). The majority of the reported cases are young men which may be due to selected materials (Reneman 1975). In the present series it occurred in 14 % of unselected patients with lower leg pain of unknown cause. Sex distribution was equal and the mean age was higher in our series than in earlier reports. The amount of exercise sufficient to provoke the symptoms may vary considerably (Reneman 1975). The walking distance varied in the present series from 200 to more than 1 500 m. The symptom duration is usually months to years by the time the diagnosis is made (Detmer 1980, Mubarak & Hargens 1981). It was three years in our series. The reason for this is undoubtedly a doctor's delay due to lack of knowledge of this disorder and that intramuscular pressure measurements are not performed. Muscle hernias are reported in 20-60 % of the cases (Reneman 1975, Mubarak & Hargens 1981). Forty per cent of the patients in our series had muscle hernias. The presence of muscle hernias may indicate that increased tension within the compartment has existed for a long time. Light manual compression on these hernias prior to exercise resulted in a considerable rise of pressure. Ischemic necrosis of the muscles in the compartment has occurred following repair of these fascial defects (Leach et al 1967, Paton 1968).

5.6. Therapeutical considerations

The treatment of compartment syndromes, whatever etiology, is decompressive fasciotomy, which allows the muscle to swell out of its tight fascial enclosure. The four muscle compartments of the lower leg are involved most frequently, the anterior tibial compartment being the most common localization of a compartment syndrome due to its tight fascial covering. Since there are no specific symptoms for compartment syndromes the only secure and objective way to make a correct diagnosis is by intramuscular pressure determination. The findings of the present investigation as well as previous studies indicate that the threshold level for a compartment syndrome is 30 mm Hg at rest. This pressure threshold is lowered by hypotension (e.g. hemorrhage) and low distal blood pressure due to arterial occlusive disease. The duration of increased pressure is also most important for the development of tissue necrosis. The time limit for an increased pressure at the level 30 mm Hg has been found to be around eight hours

(Hargens et al 1981). Thus, since timing of fasciotomy is important continuous intramuscular pressure measurement preferably with the wick technique is recommended in patients at risk of developing a compartment syndrome, e.g. in patients following distal revascularization surgery and patients with phlegmasia cerulea dolens. In these conditions fasciotomy is recommended on wide indications. In patients with venous claudication due to iliac vein obstruction and in patients with lymphedema fasciotomy may be of benefit by reducing intramuscular pressure and thereby relieving venous outflow. Fasciotomy relieves pain and normalizes intramuscular pressure, muscle blood flow and skeletal muscle metabolism in patients with a chronic anterior tibial compartment syndrome. Apart from fasciotomy diuretic treatment of three patients with chronic anterior tibial compartment syndromes (Christenson et al 1979) and treatment with mannitol (Mubarak & Hargens 1981) in experimentally induced compartment syndromes by tourniquet ischemia have been tried with good effects in order to reduce extra- and intracellular edema. Further studies are needed to evaluate these findings.

6. GENERAL SUMMARY AND CONCLUSIONS

* A standardized procedure for measurement of intramuscular (intracompartmental) pressure with the wick technique was developed

* Reference values for intramuscular pressure at rest, and during and after exercise were obtained

* An increased intramuscular pressure was found in DVT, venous claudication, intermittent claudication, lymphedema and following femoral and popliteal arterial revascularization procedures as well as in chronic compartment syndromes

* The swelling of the leg seen in venous claudication, DVT including phlegmasia cerulea dolens, lymphedema and following arterial revascularization procedures is correlated to the elevation of intramuscular pressure

* An increased intramuscular pressure resulted in an increased deposition of platelets onto femoral artery vascular grafts in an animal experimental model of a compartment syndrome

* The development of a compartment syndrome as the cause of early graft failure following distal revascularization procedures is probably underestimated

* A chronic compartment syndrome was found in 14 % of patients with lower leg pain of unknown cause

* Analysis of muscle biopsies revealed that an increased intramuscular pressure can be explained by an increased muscle water content

* An increased intramuscular pressure resulted in a decreased muscle blood flow and increased muscle lactate concentrations

* Intramuscular pressure measurement is important in the evaluation of iliofemoral thrombosis with phlegmasia cerulea dolens, venous claudication, distal revascularization procedures and the chronic compartment syndrome

* Fasciotomy is often indicated in iliofemoral thrombosis with phlegmasia cerulea dolens, in distal revascularization procedures and always in acute and chronic compartment syndromes

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Reference values for intramuscular pressure in the lower leg in man

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Summary. Intramuscular pressures in the anterior tibial and superficial posterior compartments of the lower leg were measured by the wick catheter technique in 34 healthy individuals (17 males and 17 females, mean age 42 years). The pressures were measured at rest, during and after exercise and during venous and arterial occlusion. The pressure was 1·1 (range 0·3–3·0) kPa in the anterior tibial and 0·5 (range 0·0–2·0) kPa in the superficial posterior compartment at rest. During exercise the intramuscular pressures rose to 3·5 (range 1·0–8·0) kPa and 0·9 (range 0·1–2·8) kPa respectively. The anterior tibial compartment pressures were lower in females than in males at exercise and lower in older than in younger persons at rest. After exercise the pressures were back to the pre-exercise levels within 5 min. Venous occlusion caused an increase in the pressure which was more marked in the anterior tibial compartment than in the superficial posterior compartment. Arterial occlusion did not cause any dramatic changes in intramuscular pressures, but there was a slight elevation during the period of reactive hyperaemia.

Introduction

Intramuscular pressure recordings are used clinically in the diagnosis of acute and chronic compartment syndromes. A compartment syndrome is a condition in which increased pressure within a compartment compromises the circulation to the tissues within that space (Matsen, 1975; Rorabeck & Macnab, 1975). Acute compartment syndromes are well recognized and have been extensively documented (Volkmann, 1881; Horn, 1945; Hughes, 1948; Blandy & Fuller, 1957; Seddon, 1966; Leach, Hammond & Stryker, 1967; Whitesides *et al.*, 1975, Rorabeck & Macnab, 1975, Mubarak *et al.*, 1978). Chronic or recurrent compartment syndromes have been described (Mavor, 1956; French & Price, 1962; Leach, Hammond & Stryker, 1967; Kenelly & Blumberg, 1962; Reneman, 1975; Garfin, Mubarak & Owen, 1977).

In cases with a chronic compartment syndrome the intramuscular pressure is abnormally raised during and after exercise (Reneman, 1975; French & Price, 1962). The

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pathophysiology is not known. Arterial (Griffiths, 1940; Horn, 1945; Hughes, 1948; Kinmonth, 1952; Freedman & Knowles, 1959) and venous (Murphy, 1914; Brooks, 1922; Leach, Hammond & Stryker, 1967; Paton, 1968) obstruction may be of importance for the development of compartment syndromes.

There are only a few studies of normal intramuscular pressures in man. The needle method was used by Whitesides *et al.* (1975), Reneman & Jageneau (1973), Matsen *et al.* (1976) and Brooker & Pezeschki (1979). Disadvantages with this method were blockage of the needle and the inability to perform continuous pressure recordings. With the development of the wick catheter (Mubarak *et al.*, 1976) these problems have been overcome.

The aim of the present study was to obtain reference values for intramuscular pressures at rest, during and after physical exercise in healthy individuals of both sexes at different ages. The alterations in intramuscular pressures following venous and arterial occlusion were also estimated since arterial and venous disease is known to influence intramuscular pressures.

Material and methods

Thirty-four healthy volunteers were examined. Seventeen were female and 17 were male subjects with an age from 20 to 75 (mean 42) years.

The wick catheter technique was used to measure intramuscular pressure. In the wick catheter fibrils protrude from the bore of the catheter to prevent an obstruction of the catheter. The wick catheter was introduced through a 16-gauge epidural needle into the muscle compartment under local anaesthesia. Thereafter the epidural needle was removed leaving the wick catheter in place.

The pressures were recorded with an electromagnetic transducer and recorder (Siemens Elema, Sweden). The zero level was taken on the level of the tip of the catheters (see also below). The catheters were filled with sterile heparinized saline. The pressures within the anterior tibial and superficial posterior compartments in the right or the left leg were measured at rest with the subject in a sitting position. The leg was kept horizontal. Compartment pressures were then measured at a maximal workload for 7 min. The exercise consisted of isometric activation of dorsiflexors and plantarflexors of the foot every second. The foot was attached to an isometric exerciser and the workload was continuously monitored by a dynamometer connected to a recorder only to verify that the work was constant during the exercise (Fig. 1). Since the level of the tip of the catheter in the superficial posterior compartment was about 5 cm below that in the anterior tibial compartment, the exercise had to be repeated twice with an interval of 20 min to allow for adjustment of the zero level. After exercise the intramuscular pressure was followed for 5 min. When the pressure had returned to the pre-exercise level, venous occlusion was applied in 10 patients by means of a thigh cuff immediately inflated to a pressure of 6·6 kPa (50 mmHg) for 4 min and the compartment pressures in the lower leg were

Fig. 1. Experimental set-up for measurement of intramuscular pressure in the lower leg. Wick catheters attached to pressure transducers are placed in anterior tibial and superficial posterior compartments. The foot is attached to an isometric exerciser.

measured. Thereafter, arterial occlusion was applied for 3 min by means of a thigh cuff immediately inflated to a pressure of 33·2 kPa (250 mmHg) and the compartment pressures of the lower leg were measured.

Results

The pressures in 68 compartments of 34 volunteers were measured. The compartment pressures in the anterior tibial and superficial posterior compartments at rest and during exercise are shown in Table 1. At rest the tissue pressure was significantly ($P<0·001$) higher in the anterior tibial, 1·1 (range 0·3–3·0) kPa, compared to the superficial posterior compartment 0·5 (range 0·0–2·0) kPa. During exercise the tissue pressure rose to a significantly ($P<0·001$) higher level in the anterior tibial, 3·5 (range 1·0–8·0) kPa, compared to the superficial posterior compartment, 0·9 (range 0·1–2·8) kPa. The pressure in the anterior tibial compartment declined to 1·3 kPa one min after exercise. After 5 min all pressures were back to the pre-exercise rest levels. In the superficial posterior compartment the pressures were back to the pre-exercise level already within 1 min (Fig. 2).

The time period for the pressure to reach half-way back to the initial resting pressure after exercise (T 1/2) was estimated. It was 3 ±4·0 s in the anterior tibial compartment

Table 1. Intramuscular pressures (kPa) in the anterior tibial and the superficial posterior compartments in 34 normal persons at rest and during exercise (range values within brackets)

	Total (n = 34)	Male (n = 17)	Female (n = 17)
Anterior tibial compartment			
At rest	1·1 (0·3–3·0)	1·3 (0·5–3·0)	1·0 (0·3–2·0)
At work	3·5 (1·0–8·0)	4·4 (1·1–8·0)	2·7 (1·0–6·4)
Superficial posterior compartment			
At rest	0·5 (0·0–2·0)	0·6 (0·0–2·0)	0·4 (0·0–1·7)
At work	0·9 (0·1–2·8)	1·1 (0·3–2·9)	0·7 (0·1–2·2)

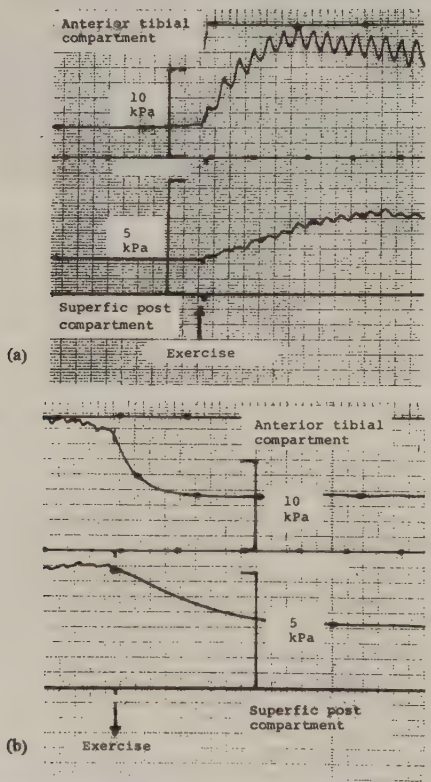

Fig. 2. Anterior tibial and superficial posterior compartment pressure curves at rest and at the beginning of exercise (a) and at the end of exercise (b) in two controls.

and $1 \pm 1{\cdot}0$ s in the superficial posterior compartment. The anterior tibial compartment pressures at exercise were significantly ($P<0{\cdot}02$) lower in the females than in the males. The anterior tibial pressures were significantly ($P<0{\cdot}001$) lower in older than in younger persons at rest. In the superficial posterior compartment no significant relationship to age was demonstrated.

Venous occlusion initiated an increase of the intramuscular pressure. This increase of pressure was significantly ($P<0{\cdot}001$) more marked in the anterior tibial, $1{\cdot}4 \pm 0{\cdot}86$ kPa than in the superficial posterior compartment, $0{\cdot}5 \pm 0{\cdot}26$ kPa (Fig. 3). The intramuscular pressure remained nearly unaffected by short-term ischaemia but there was as light elevation during the period of reactive hyperaemia (Fig. 4).

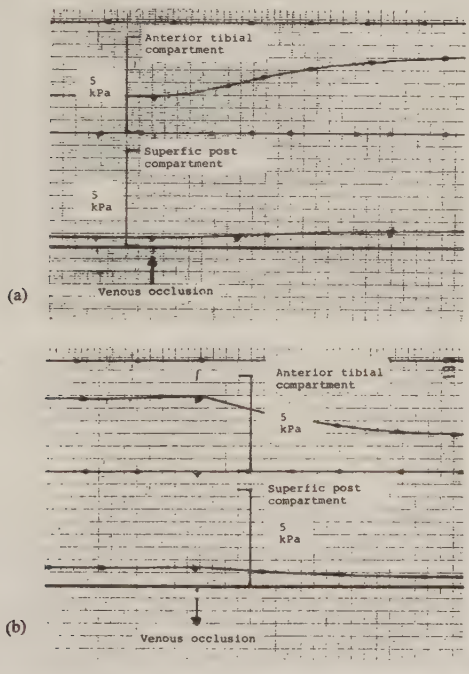

Fig. 3. Anterior tibial and superficial posterior compartment pressure curves at the beginning of venous occlusion (a) and at the end of venous occlusion (b). Venous occlusion pressure 6·6 kPa by a thigh cuff inflated for 4 min.

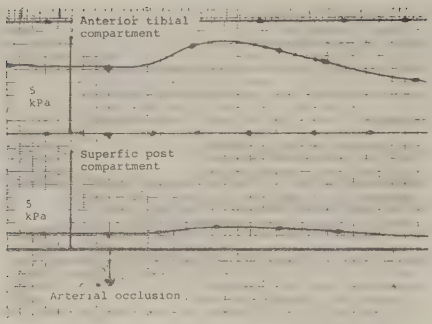

Fig. 4. Anterior tibial and superficial posterior compartment pressure curves at the end of arterial occlusion for 3 min.

Discussion

There are only a few studies of normal intramuscular pressures in man. French (1962) and Reneman (1975) used the needle method in the anterior tibial compartment. The needle method is considered to be less exact than the wick catheter method and it does not allow continuous pressure recordings during muscle contraction (Mubarak *et al.*, 1976). Continuous recordings of intramuscular pressure during and after exercise is probably important in the diagnosis of a chronic compartment syndrome. In our hands the wick catheter technique was found to be a convenient method for measuring intramuscular pressure. There was no blockage of the catheters and continuous recordings were possible.

The normal resting pressure in the anterior tibial compartment and in the flexor muscles of the forearm in 23 volunteers averaged 4 ± 4 mmHg ($0{\cdot}5 \pm 0{\cdot}5$ kPa) with the wick catheter technique (Mubarak *et al.*, 1976). With the same technique in the present study the corresponding value for the anterior tibial compartment is higher, 1·1 (range 0·3–3·0) kPa.

The present results showed that the intramuscular pressure was higher in the anterior tibial compartment at rest as well as during exercise and venous occlusion than in the superficial posterior compartment. Wells *et al.* (1938) also found higher resting pressure in the anterior tibial compartment than in the gastrocnemius. One reason for this may be that the anterior tibial compartment is more rigid than the superficial posterior compartment. In preliminary experiments we have found that the intramuscular pressure is higher in the anterior tibial compartment than in the superficial posterior compartment also in the supine position (unpublished observations). This may indicate that the pressure difference in the sitting position is not due to differences in muscular tension between the two compartments.

In the present investigation it was found that the normal intramuscular pressure was lower in older than in younger persons and lower in females than in males which correlates with earlier findings (Reneman & Jageneau, 1973). This is probably due to the difference in tissue elasticity and muscle volume.

Venous hypertension and arterial occlusion or spasm has been proposed to be an aetiological factor in the anterior tibial compartment syndrome but this concept is not favoured today (French & Price, 1962; Matsen, 1975). In the present investigation in healthy volunteers it was found that venous and arterial occlusion for a few minutes caused only minor and short-lasting increases of intramuscular pressure. During venous occlusion the intramuscular pressure did not reach the level of the occlusion pressure. The modern concept is that the raised intramuscular pressure in compartment syndromes is secondary to an abnormally raised extravascular hyperosmolarity (Lundvall, 1972; Rorabeck & Macnab, 1975; Hargens *et al.*, 1978).

In the diagnosis of chronic compartment syndromes Reneman (1975) used remaining pressure increment over the resting value rather than absolute pressure values. In patients with a chronic compartment syndrome it takes a long time—sometimes more than an hour—before the pressure is back to the pre-exercise level (French & Price, 1962). In the present study the time period for the pressures to reach half-way back to the initial resting pressure after exercise (T 1/2) was very short, usually only a few seconds or less in the compartments of the lower leg. In all the normal persons the presssures were back to the pre/exercise level within 5 min. T 1/2 may be a useful index of pressure return time to the initial rest level after exercise.

The pressure values of the anterior tibial and superficial posterior compartments in volunteers obtained in this study will be used as reference values in the clinical evaluation of patients with suspected acute and chronic compartment syndromes.

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INTRAMUSCULAR PRESSURE IN THE LOWER LEG IN DEEP VEIN THROMBOSIS AND PHLEGMASIA CERULEA DOLENS.

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Running title: Intramuscular pressure in DVT

Abstract

The influence of deep vein thrombosis on intramuscular pressure was evaluated in 22 patients by means of the wick technique. Intramuscular pressure was measured in the anterior tibial and the deep posterior compartments in both legs before and during treatment. The intramuscular pressure was significantly ($p<0.001$) higher in the thrombosed leg than in the contralateral leg (0-16 mm Hg). The increase in intramuscular pressure was related to the extension of the thrombus. Iliofemoral thrombosis caused a significantly ($p<0.001$) higher pressure (17-28 mm Hg) than calf thrombosis (16-23 mm Hg). A compartment syndrome was found to be a part of the entity phlegmasia cerulea dolens (rest pressure 47-56 mm Hg). In the treatment of phlegmasia cerulea dolens fasciotomy is suggested additional to other therapeutical procedures.

Key words: Intramuscular pressure, deep vein thrombosis, iliofemoral thrombosis, phlegmasia cerulea dolens.

Introduction

Deep vein thrombosis may produce calf swelling, tenderness and stretch pain (Homans´sign). These symptoms are also seen in other conditions such as cellulitis, stress fracture, tenosynovitis and acute and chronic compartment syndromes. The differential diagnosis may be difficult, requiring phlebography and intramuscular pressure recordings.[1] Deep vein thrombosis is an uncommon cause of a compartment syndrome except inits more severe form, phlegmasia cerulea dolens.[1] Phlegmasia cerulea dolens is a condition with massive venous thrombosis. Experimental studies have shown that the massive intravenous thrombosis in phlegmasia cerulea dolens may be sufficient to cause nearly complete arrest of capillary blood flow.[2-5] The critical intramuscular pressure when this occurs is 30 mm Hg.[6] Gangrene follows when an increased intramuscular pressure reaches the critical closing pressure of the small peripheral arteries.[4, 7] This is a result of increasing interstitial (intramuscular) pressure.[3, 4, 6] Intramuscular pressure has so far not been determined in deep vein thrombosis and phlegmasia cerulea dolens in man. This study estimates intramuscular pressure in deep vein thrombosis including phlegmasia cerulea dolens to see whether there was a correlation between intramuscular pressure and the severity of clinical and phlebographic findings.

Methods

Twenty-two patients, 8 males and 14 females, with a symptomgiving unilateral deep vein thrombosis were studied. The patients were selected at random. Their mean age was 63 (range 34-82) years. The diagnosis was

established by phlebography. Ten patients had a calf thrombosis and 12 patients had an iliofemoral thrombosis continous with calf thrombosis. The patients with calf thrombosis had mild pain and swelling of the calf, three had a positive Homans´test. Eight patients with iliofemoral thrombosis had moderate pain and swelling of the whole leg. Homans´test was positive in four cases. Four patients with an iliofemoral thrombosis presented with the classical symptoms of phlegmasia cerulea dolens: Sudden excrucial pain, massive edematous swelling of the whole leg, blue discolouration, absence of peripheral pulsations and signs of dehydration. The symptoms and signs of the 22 patients are listed in Table I.

I. Phlebography

Antegrade and retrograde femoral phlebography was performed according to Gullmo[8] using contrast medium Conray Meglumine 282 (Astra Meditec, Sweden). In cases with iliofemoral thrombosis femoral phlebography on the contralateral leg was performed to visualize the upper limit of the thrombus.

II. Intramuscular pressure measurement

The wick catheter technique[9-10] was used to measure intramuscular pressure. The pressure was measured in the anterior tibial and deep posterior compartments in both legs in the supine patient at rest and during a few seconds of passive tension of the calf muscles (Homans´maneuver). The healthy leg served as a control.

TABLE I.

Patient material with regard to type of thrombus, leg swelling and Homans´sign. Calf and thigh swelling is expressed as increase in circumference (cm) compared with the contralateral leg.

Type of thrombus	No	Calf swelling (cm, mean ± SD)	Thigh swelling (cm, mean ± SD)	Homans´sign
Calf	10	1.7 ± 0.6	--	3
Iliofemoral	8	3.9 ± 1.1	4.6 ± 2.0	4
Iliofemoral with phlegmasia cerulea dolens	4	9.1 ± 1.8	12.3 ± 2.4	4

The pressures were measured on the day of admission immediately after the phlebography and before treatment. The pressures were then measured daily for 4 days.

III. Treatment

Anticoagulant therapy. Heparin was administered in all patients. Patients with iliofemoral thrombosis were treated with 40 000 IE heparin daily in continous i.v. infusion during five days. In patients with calf thrombosis 5 000 IE heparin was given six times a day for three days. An antiprothrombinolytic drug (Dicumarol) was given per os.

Surgical therapy. Eight patients (including three patients with phlegmasia cerulea dolens) with an iliofemoral thrombosis were operated upon. A venous thrombectomy and a temporary AV-fistula for 6 weeks to prevent rethrombosis was carried out. The four patients with phlegmasia cerulea dolens were given i.v. infusions of blood, plasma and Ringer lactate to combat dehydration and shock.

Elevation of the leg to 45 degrees for one day in calf thrombosis and for three days in iliofemoral thrombosis and bandaging of the whole leg were used as a routine in all cases.

RESULTS

The intramuscular pressures in 88 compartments of 44 legs in 22 patients were measured.

Control leg

The intramuscular pressure was 6 (range 2-16) mm Hg in the anterior tibial compartment and 3 (range 0-11) mm Hg in the deep posterior compartment. During passive tension of the calf muscles (Homans' manoeuver) the pressure increased significantly ($p < 0.001$) to 7 (range 3-17) mm Hg in the deep posterior compartment.

Calf thrombosis

A minor though significant ($p < 0.001$) increment in both the anterior tibial, 15 (range 7-23 mm Hg and deep posterior compartment, 11 (range 6-23) mm Hg was seen. Passive dorsiflexion of the ankle made pressure rise ($p < 0.001$)to 20 (range 10-30) mm Hg in the deep posterior compartment (Fig. 1). After treatment the intramuscular pressure was normalized within 24 hours (Fig. 2).

Iliofemoral thrombosis

The increment of pressure was more pronounced ($p < 0.001$) in iliofemoral thrombosis than in calf thrombosis. Thus the pressure rose to 26 (range 21-28) mm Hg in the anterior tibial and to 23 (range 17-26) mm Hg in the deep posterior compartment. During Homans' manoeuver the pressure rose ($p < 0.01$) to 30 (range 20-42) mm Hg in the deep posterior compartment (Fig. 1). After treatment the intramuscular pressure

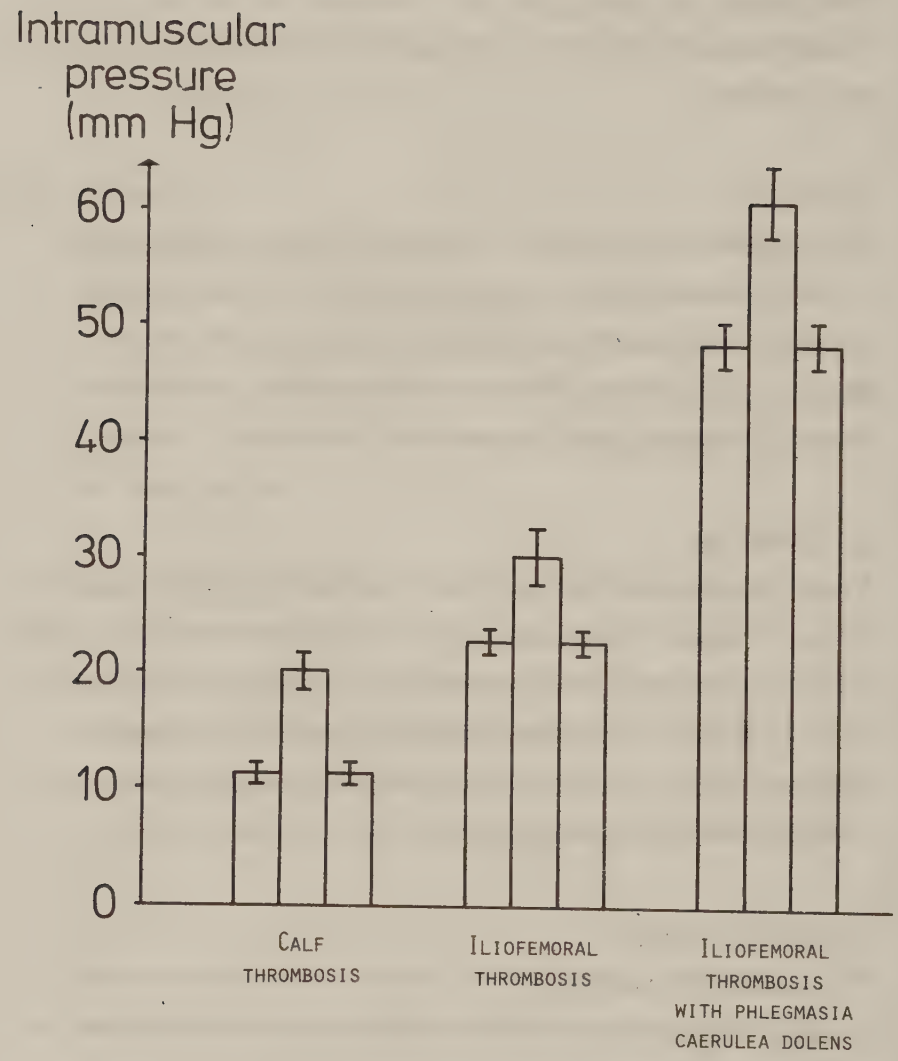

Fig. 1. Intramuscular pressure (mean ± SEM) in the deep posterior compartment before, during and after Homans' manoeuver in patients with calf vein thrombosis (n=10), iliofemoral thrombosis (n=8) and iliofemoral thrombosis with phlegmasia cerulea dolens (n=4).

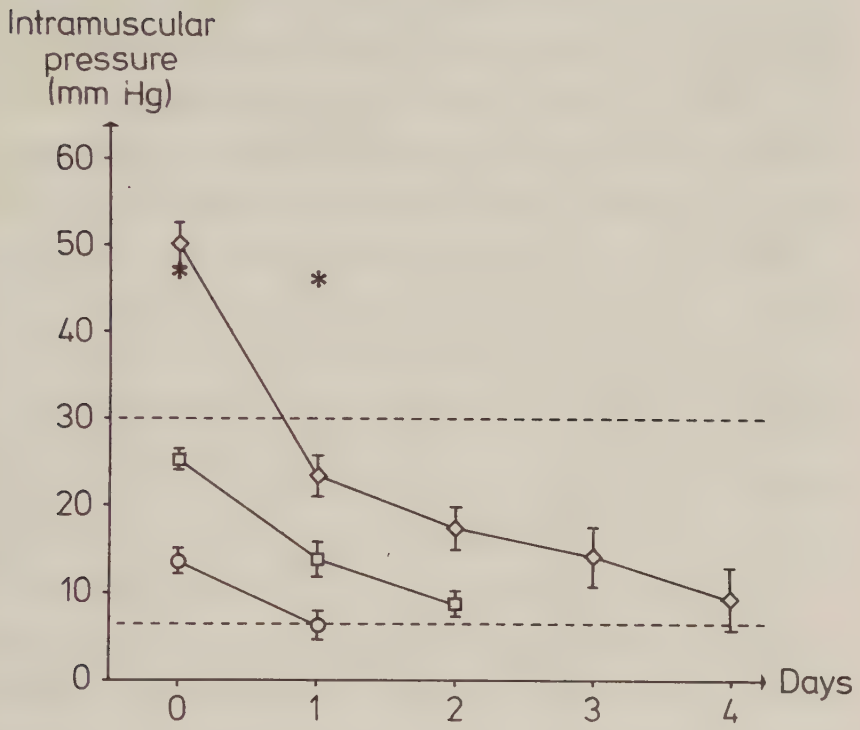

*Fig. 2a. Intramuscular pressure (mean ± SEM) in the anterior tibial compartment in calf vein thrombosis (○—○, n = 10), iliofemoral thrombosis (□—□, n = 8) and iliofemoral thrombosis with phlegmasia cerulea dolens (◇—◇, n = 3) before and during treatment. * represents one patient with iliofemoral thrombosis with phlegmasia cerulea dolens who developed gangrene. Upper and lower horizontal interrupted lines indicate "critical" and normal intramuscular pressure.*

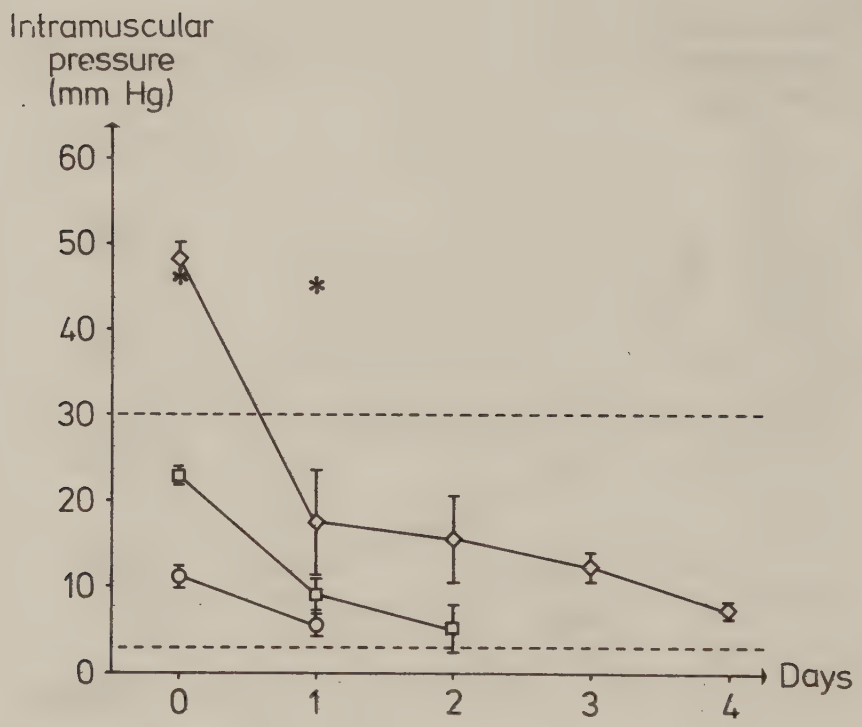

Fig. 2b. Intramuscular pressure (mean ± SEM) in the deep posterior compartment in calf vein thrombosis (n = 10), iliofemoral thrombosis (n = 8) and iliofemoral thrombosis with phlegmasia cerulea dolens (n = 3) before and during treatment. (Symbols as in Fig. 2a.)

was normalized within 48 hours (Fig. 2).

Iliofemoral thrombosis and phlegmasia cerulea dolens

Markedly elevated ($p < 0.001$) pressure values were noted, 50 (range 47 - 56) mm Hg in the anterior tibial and 48 (range 47-52) mm Hg in the

deep posterior compartment. During Homans´manoeuver the pressure rose ($p = < 0.05$) to 61 (range 53-68) mm Hg in the deep posterior compartment (Fig. 1). After treatment the intramuscular pressure was gradually normalized within 4 days in all but one case (Fig. 2). This patient with phlegmasia cerulea dolens had a history of intermittent claudication. He did not improve after venous thrombectomy but deteriorated after 24 hours with increasing pain and no palpable distal pulsations in the leg. Intramuscular pressure remained markedly elevated, 47 mm Hg, in the anterior tibial and 46 mm Hg in the deep posterior compartment. The patient was reoperated to restore arterial blood flow. At reoperation a Fogarty catheter was passed into the femoral artery and down to the ankle but no thrombi were found, and blood flow did not improve. A femoro-popliteal artery by-pass reconstruction was performed together with a fasciotomy. The graft occluded immediately postoperatively and the patient had finally a femoral amputation due to gangrene of the lower leg.

Discussion

Occlusion of the femoral vein in dogs causes a syndrome essentially identical to phlegmasia cerulea dolens in man.[4, 11-13] The classical signs and symptoms of pain, cyanosis, shock, massive edema, loss of pulses and venous gangrene are all present. The venous occlusion is followed by a marked increase in intramuscular pressure to about 40 mm Hg.[4, 11] This means that the pressure difference across the arterial wall in the extremity decreases to 15-20 mm Hg. Burton[7] has

stated that the "critical closing pressure" for arteries is approximately 20 mm Hg. This explains why loss of arterial pulsation or abolished arterial blood flow is observed after venous occlusion. [4.12-13] Hargens et al[6] concluded that capillary perfusion is reduced at an intramuscular pressure of 30 mm Hg. In the present investigation it was found that the intramuscular pressure in calf vein thrombosis and in iliofemoral thrombosis was below 30 mm Hg. This agrees with the hupothesis by Mubarak and Hargens[1] that deep vein thrombosis is an uncommon cause of a compartment syndrome. In iliofemoral thrombosis causing phlegmasia cerulea dolens, on the other hand, we found markedly increased intramuscular pressures well above 300 mm Hg. This means that a compartment syndrome in the lower leg is a part of the entity phlegmasia cerulea dolens. The present data showed that the increment of intramuscular pressure was correlated to the extension of the thrombus. Therefore, it seems logic that the massive venous thrombosis in conneciton with phlegmasia cerulea dolens [5, 14] is followed by a pronounced increase in intramuscular pressure. It has previously been shown that also proximal venous occlusion in healthy controls raises the intramuscular pressure in the lower leg.[10]

Pain is one of the classical signs in phlegmasia cerulea dolens. The pain is very likely due to the increased intramuscular pressure which leads to ischemia. Similarly, Mubarak et al[9] registered that patients undergoing osteotomy felt pain when the intramuscular pressure reached approximately 30 mm Hg. In the present study it was noted that passive dorsiflexion of the foot (Homans' manoeuver) caused pain in

patients with deep vein thrombosis when there was a marked short-lasting increase in intramuscular pressure. This finding indicates that pain in connection with high intramuscular pressure is not only due to ischemia. It seems resonable to assume that the pressure increase also might activate pain receptors.

Different therapeutical approaches have been tried for phlegmasia cerulea dolens (see Bülow & Sager [5], Brockman & Vasko[15]). Venous thrombectomy appears to be the most specific form of treatment since venous outflow is restored. Venous thrombectomy has also given the best results.[16-21] Venous thrombectomy with an AV-fistula was used in three of the four patients with phlegmasia cerulea dolens in the present series. Two patients had an uneventful postoperative period and were completely recovered. Intramuscular pressure showed normal values 4 days after operation. The third patient was initially well after venous thrombectomy but then underwent an unsuccessful course and was finally amputated. It should be noted that the intramuscular pressure remained high in this patient. One can only speculate whether the outcome would have been different if fasciotomy had been performed in the early course along with the venous thrombectomy. Fasciotomy may be of benefit by reducing intramuscular pressure and thus decrease the pressure differance across the wall of the artery, allowing a greater arterial inflow. Fasciotomy has been recommended by some outhors.[3, 18, 22-23] Elastic bandaging of the leg was also used in the four patients. This treatment has been questioned.[12, 15] It should be noted. however, that the fourth patient in the present series was treated with heparin,

elastic bandaging and elevation only with a normalized intramuscular pressure within two days and complete recovery. Anticoagulant therapy has been used to prevent further thrombosis or rethrombosis.[15] The efficacy of intravenous administration of heparin and elevation of the limb has been demonstrated.[24] Elevation to promote venous return seems to be a sound method for reducing venous engorgement.[15] Despite therapeutical efforts amputation is common, about 50%, in phlegmasia cerulea dolens and the mortality rate is about 25-30%.[15, 18] The choice of treatment, perhaps particularly early fasciotomy, may be of great importance for the amputation rate. In the present material amputation was necessary in one out of four patients. In the present series it has been shown that intramuscular pressure is increased in DVT. The increment of the intramuscular pressure in the lower leg is dependent on the extension of the thrombus. Thus, there is a very marked increase of the intramuscular pressure in iliofemoral thrombosis with phlegmasia cerulea dolens, causing av compartment syndrome. In these cases intramuscular pressure measurements are suggested to evaluate the need for fasciotomy.

Acknowledgment

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INTRAMUSCULAR PRESSURE, BLOOD FLOW AND SKELETAL MUSCLE METABOLISM IN PATIENTS WITH VENOUS CLAUDICATION

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Abstract

Nine patients with chronic iliac vein obstruction and venous claudication were investigated. Intramuscular pressure was measured in the anterior tibial and the deep posterior compartments in both legs at rest and during exercise. The pressures were significantly higher in the leg with iliac vein obstruction, 39 $\pm$ 10 mm Hg, than in the contralateral leg, 26 $\pm$ 12 mm Hg at rest as well as during exercise, 60 $\pm$ 16 mm Hg and 41 $\pm$ 15 mm Hg, respectively, in the deep posterior compartment. Similar changes were observed in the anterior tibial compartment. Muscle water content was higher ($p < 0.01$) in the obstructed leg and contributes to explain the high intramuscular pressure in this leg. Muscle blood flow, ATP, CP and lactate were determined in the gastrocnemius muscles at rest and exercise. Muscle blood flow, measured with the ^{133} Xenon clearance technique was lower in the obstructed leg, 17.5 ml/min, 100 g than in the control leg, 28.1 ml/min, 100 g during exercise. Lactate increased more ($p < 0.05$) in the obstructed leg. It is suggested that pain in venous claudication is caused by the high intramuscular pressure and therefore fasciotomy may be useful in the treatment of this disorder.

Introduction

Chronic iliac vein obstruction follows iliac vein thrombosis with inadequate recanalization and inadequate collateral formation.[3,5,6,9,16] Swelling of the whole leg is present. A common symptom is venous claudication with bursting pain in the leg during exercise. Venous claudication occurs in this group only and is not present in patients with valvular incompetence or with postthrombotic involvement of the peripheral deep veins alone.[6] The mechanism of pain is not known. The possibility of increased intramuscular pressure[1] or muscle ischemia[12] has been mentioned. It has previously been shown that venous occlusion and deep vein thrombosis cause an elevation of intramuscular pressure.[13] Intramuscular pressure has not previously been assessed in patients with chronic iliac vein obstruction and venous claudication. The present study was designed to determine intramuscular pressure in such patients and to assess the effects of changes in intramuscular pressure. Leg muscle blood flow was studied with 133 Xenon clearance technique and muscle metabolite and water contents of biopsies from the gastrocnemius muscle were studied before and after exercise provoking venous claudication.

Material

Nine patients (one male and 8 females) aged 18 to 80 (mean 42) years were studied. All had a previous history of unilateral iliofemoral thrombosis 2 - 43 (mean 8) years ago. The left leg was affected in 8 cases. At the time of thrombosis all were treated with anticoagulants (heparin and dicumarol). Two patients in addition to anticoagulant therapy underwent a venous thrombectomy with temporary arteriovenous fistula. At the time of the investigation all patients suffered from serious postthrombotic symptoms. All had considerable leg swelling with a calf circumference increased by 4.5 $\pm$ 2.1 cm compared to the contralateral leg. Lower leg varicose veins appeared in 6 patients. Three of these also had chronic ulceration of the ankle. Dilated collateral veins in the groin and lower abdomen were observed in 2 patients. Venous claudication was a constant symptom in all 9 patients. Walking distance was limited with a stop limit of 514 $\pm$ 255 m (mean $\pm$ SD), symptoms beginning after 223 $\pm$ 201 m. The systolic blood pressure of the big toe measured with strain gauge technique was normal in all subjects when compared to systolic blood pressure in the arm. Furthermore, there was no significant difference between the obstructed and the contralateral legs. Peripheral pulses of the posterior tibial and dorsal pedis arteries were normal in all patients. Phlebography performed according to Gullmo[7] showed complete occlusion of the left iliac vein in 8 patients and of the right iliac vein in one patient. Femoral venous pressure measurement showed a significant ($p < 0.05$) gradient between the occluded and the contralateral leg at rest, 4.0 $\pm$ 1.0 mm Hg

as well as during exercise, 7.1 ± 2.1 mm Hg.

Methods

Intramuscular pressure measurement was performed in all nine patients using the wick technique as described in a previous paper[13]. The wick catheters were placed into the anterior tibial and the deep posterior compartments under local anesthesia. The pressures were recorded with an electromagnetic transducer and recorder (Siemens Elema, Sweden). The zero level was taken on the level of the tip of the catheters. The catheters were placed in the muscle compartments at the same level about 15 cm below the knee joint. The compartment pressures were measured in the obstructed and contralateral leg at rest with the patient in a standing position. Compartment pressures were then measured during heel-raising every second for at least 5 min or until pain forced the patient to stop.

Muscle blood flow was measured in 5 patients in the gastrocnemius muscles bilaterally using the 133 Xenon clearance technique. The legs were studied one after the other. Approximately 3.5 MBq 133 Xenon in 0.1 ml of isotonic saline was injected into the gastrocnemius muscle about 15 cm below the knee joint at a depth of about 2 cm using a needle with 0.4 mm outer diameter. The isotope was slowly injected during 15 sec and the needle was withdrawn 15 sec thereafter. Records were taken from both legs with the patient at rest in a standing position, during heelraising 60 times per min until symptoms of

venous claudication occurred from the diseased leg and during 5 min after exercise. Counting rate versus time was recorded directly over the site of injection with a collimated cadmium telluride detector (TE 101, Pharmacia Electronics, Denmark) attached to the skin surface of the legs with adhesive tape. The detector was connected to a portable memory, Memolog-500 (Pharmacia Electronics, Denmark) working as multi-scaler giving digital information of the counting rate variation in 8 sec intervals which after each study was written directly into a computer (ABC 80). The blood flow (f) was calculated from the half-time (T1/2) of the disappearance of the isotope according to the following formula: $f = \frac{\ln 2 \cdot \lambda \cdot 60 \cdot 100}{T\,1/2}$, where λ represents the partition coefficient for 133 Xenon between tissue and blood. A standardized value of 0.7 ul/g was used for λ, since it has been used previously for muscle tissue.[8] The calculated muscle blood flow is expressed as ml/min, 100 g tissue.

Metabolic analysis: Muscle biopsies were extracted with Radner forceps (No 13717, AB Stille Werner, Stockholm, Sweden) from the gastrocnemius muscle about 15 cm beneath the knee joint under local anesthesia. The muscle biopsies were taken from the superficial posterior compartment in order to minimize the operative trauma. The biopsies were taken from both legs at rest and immediately after a maximal work load as described above causing symptoms of venous claudication from the diseased leg. The muscle specimens were immediately frozen in isopentane cooled to

freezing point and stored at -80°C until analysis. ATP, phosphocreatine (CP) and lactate were analyzed using enzymatic fluorometric technique. Total muscle water was obtained by weighing the samples before and after freeze drying.

Results

Intramuscular pressure. The intramuscular pressure in the deep posterior compartments was significantly ($p < 0.001$) higher in the leg with iliac vein obstruction, 39 ± 10 mm Hg than in the contralateral leg, 26 ± 12 mm Hg at rest as well as during exercise, 60 ± 16 mm Hg and 41 ± 15 mm Hg, respectively. In the anterior tibial compartment of the obstructed leg the intramuscular pressure rose from 35 ± 12 mm Hg at rest to 52 ± 13 mm Hg at exercise ($p < 0.001$). The corresponding values for the contralateral leg were 22 ± 8 mm Hg and 36 ± 8 mm Hg, respectively.

Muscle blood flow as determined with the 133 Xenon clearance technique did not differ significantly between the leg with venous claudication, 2.7 ± 1.2 ml/min, 100 g and the contralateral leg, 2.2 ± 1.8 ml/min, 100 g at rest. During exercise, however, muscle blood flow was significantly ($p < 0.01$) lower in the obstructed leg, 17.4 ± 3.2 ml/min, 100 gr than in the contralateral leg, 28.0 ± 3.0 ml/min, 100 g (Fig. 1). After exercise blood flow decreased to the initial rest value within 5 min in both legs.

Skeletal muscle metabolism. The results are given in Fig. 2, all values are expressed in wet weight. The phosphagen stores were low at rest in both the obstructed and the control leg. This was true both for ATP and CP. No significant difference was found between the legs. The exercise caused ATP to become reduced from its resting level of 3.3 $\pm$ 0.3 mmol/kg to 2.5 $\pm$ 0.5 mmol/kg in the control leg and from 3.2 $\pm$ 0.3 mmol/kg to 2.2 $\pm$ 0.5 mmol/kg in obstructed leg. The reduction of the ATP was significant ($p < 0.01$) for both legs. CP became reduced with the exercise from 13.6 $\pm$ 1.1 mmol/kg to 9.5 $\pm$ 0,5 mmol/kg in the healthy leg and from 12.8 $\pm$ 1.4 mmol/kg to 6.5 $\pm$ 1.5 mmol/kg in the affected leg ($p < 0.01$). Muscle lactate was low at rest both in the healthy and the affected leg with a significant increase in both legs with the exercise. The elevation was larger ($p < 0.05$) in the sick leg. Muscle water content was quite normal in the healthy leg at rest with a mean value of 76.0 %. The affected leg had a slightly higher water content of 77.3 % ($p < 0.01$). The exercise caused the water content to increase in both legs. However, the increase was slightly higher in the affected leg, 79.7 % ($p < 0.01$) than in the healthy leg, 77.5 % (not significant).

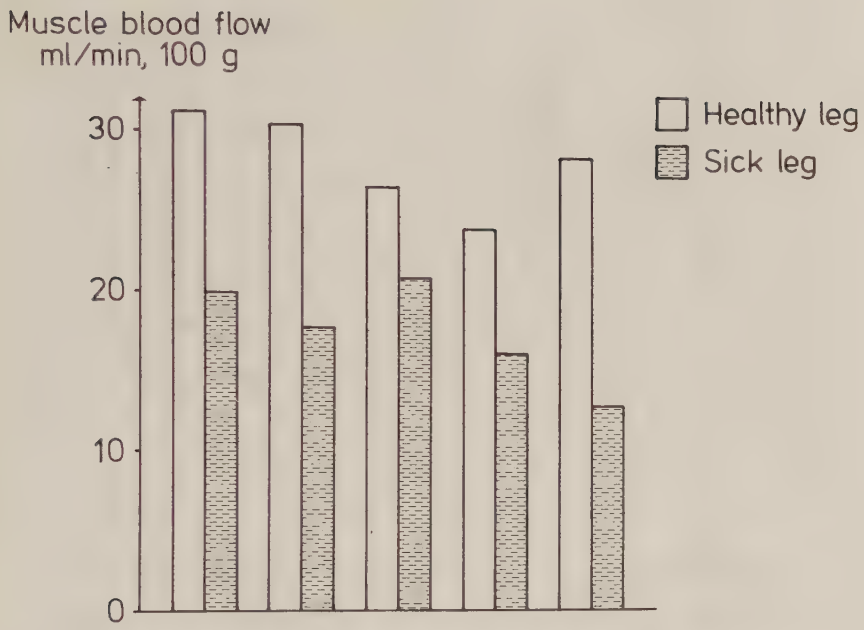
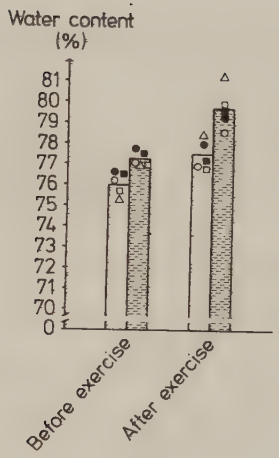
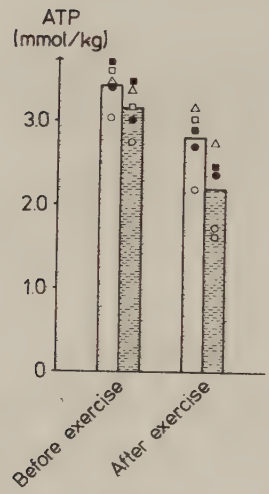
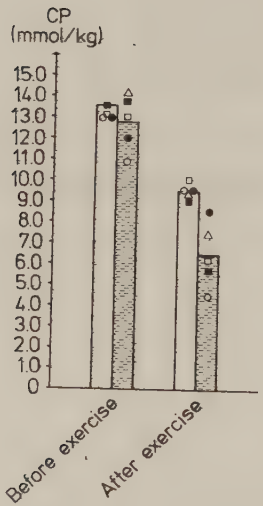


Fig. 1. Muscle blood flow during exercise in both legs of five patients with unilateral venous claudication.







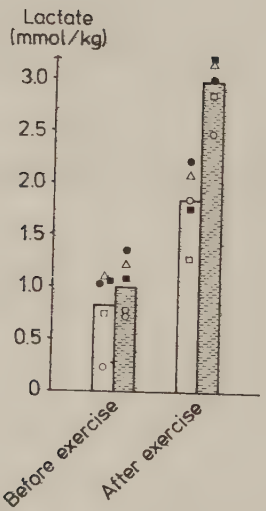


Fig. 2. Muscle water content and concentrations of ATP, CP and lactate in the gastrocnemius muscles of both legs in five patients with unilateral venous claudication before and after exercise. Similar symbols refer to the same patient.

□ *healthy leg;* ▤ *sick leg.*

Discussion

Postthrombotic iliac venous obstruction has been found to cause venous claudication, firstly described by Cockett et al in 56 cases.[5] The following criteria were set for the diagnosis of venous claudication: 1. Intermittent claudication, 2. Iliac vein obstruction, 3. Venous hypertension at rest, 4. Elevation of venous pressure at exercise. All nine patients in the present series fulfilled these criteria. Intermittent venous claudication is usually less severe than arterial claudication.[6] In the present patients the stop limit was found to be 514 $\pm$ 255 m. The mechanism of pain in this disorder is not known. The possibility that pain is produced by nociceptor stimulation of the distended vein wall has been discussed.[6] Negus [12], on the other hand, did not find any evidence that venous distension or muscle ischemia caused the pain. He proposed that the pain was due to an increased interstitial pressure or an accumulation of tissue metabolites. The possibility of increased intramuscular pressure as an explanation of the pain in patients with venous claudication was tested in the present study by lower leg intramuscular pressure measurements at rest and during exercise. The intramuscular pressure was found to be markedly elevated in both the anterior tibial and the deep posterior compartment of the obstructed leg. Venous occlusion has previously been shown to cause a rise in intramuscular pressure in both experimental models[4,15] and in humans.[13] The elevated intramuscular pressure is thought to be due to an increased transudation of fluid into the surrounding tissue during venous occlusion.[17] A similar transudation of fluid might occur in patients with venous claudication. This hypothesis was strengthened by the present finding that

the muscle water from the gastrocnemius muscles was more elevated in the leg with venous claudication both at rest and immediately after exercise. The increased muscle water content probably contributes to explain the higher intramuscular pressure in the leg with iliac vein obstruction. It should be noted that estimations of intramuscular pressure were performed in the anterior tibial and the deep posterior compartments, while muscle biopsies and estimation of blood flow were carried out in the superficial posterior compartment for practical reasons. It seems likely that metabolic changes and changes in muscle water and blood flow in the superficial posterior compartment reflect similar changes in the other compartments of the leg. Furthermore, it seems likely that changes in intramuscular pressure of the anterior tibial and the deep posterior compartments reflect similar changes in the intramuscular pressure of the superficial posterior compartment. It has previously been shown, that acute venous occlusion causes an increased intramuscular pressure in the superficial posterior and the anterior tibial compartments, although the pressure increase is more marked in the anterior tibial compartment.[13]

An increased interstitial pressure may lead to a compression of the distal end of capillaries and as a consequence a reduced capillary blood flow.[17] Many investigators[2,14,17] have demonstrated that increased intramuscular pressure reduces muscle blood flow. This was also true in the present study where muscle blood flow during exercise as measured with the 133 Xenon technique was significantly decreased in the leg with

venous claudication and with increased intramuscular pressure. Metabolic analysis of samples from the gastrocnemius muscles of both the obstructed and the contralateral legs before and immediately after exercise revealed a more pronounced elevation of lactate in the sick leg. This finding may be explained by the decreased muscle blood flow that was found in the leg with venous claudication. The lactate concentrations were, however, remarkably low in both legs immediately after exercise and are not likely to limit work performance. The low concentrations of ATP and CP at rest could be explained by a decreased blood perfusion in the gastrocnemius muscles of both legs but the patients had no signs of arterial occlusive disease. Peripheral pulses and systolic blood pressure of the big toe were normal in both legs. There was a normal depletion of the phosphagen stores immediately after exercise in both legs.

In conclusion the present study shows that intramuscular pressure is elevated in patients with iliac vein obstruction and venous claudication. This increment of intramuscular pressure causes a decreased muscle blood flow during exercise. It seems unlikely that this relative ischemia or the accumulation of lactate is responsible for the pain in venous claudication. It has been shown that increased intramuscular pressure causes pain.[10,11] Therefore it seems likely that pain in venous claudication is caused by the increased intramuscular pressure demonstrated in the present study. Fasciotomy has been of great benefit to relieve pain and reestablish function in other conditions with elevated intramuscular pressure such as compartment syndromes of

different etiology.[10] Therefore it seems likely that fasciotomy might be of value in the treatment of venous claudication. Studies need to be done to evaluate fasciotomy as a therapeutical procedure in patients with venous claudication.

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INTRAMUSCULAR PRESSURE IN THE CLAUDICANT LEG

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SUMMARY

Intramuscular pressure in the anterior tibial and superficial posterior compartments was determined using the wick technique in 10 patients with intermittent claudication and in 10 healthy subjects at rest, during and after exercise. Intramuscular pressures did not differ significantly between the two patient groups at rest. During exercise the intramuscular pressures were significantly ($p < 0.001$) higher in the claudicant group in both the anterior tibial, 30 ± 6 mm Hg and the superficial posterior compartment, 14 ± 3 mm Hg, than in the healthy subjects, 24 ± 5 mm Hg and 7 ± 2 mm Hg, respectively. The elevated intramuscular pressure seen in patients with intermittent claudication during exercise may contribute to impair tissue blood perfusion and aggravate ischemic pain.

ZUSAMMENFASSUNG

Messungen der Muskeldrücke mit der Wick-katheter-Methode in der Tibialis-anterior-Loge und in der oberflächlichen hinteren Muskelloge von 10 Patienten mit claudicatio intermittens und 10 Kontrollpersonen wurden im Ruhezustand, kontinuerlich während und nach den Muskelkontraktionen ausgefü hrt. Im Ruhezustand gab es keinen signifikanten Druckunderschied zwischen den beiden Gruppen. Während der Muskelkontraktionen waren die Muskeldrücke bei den Klaudikanten jedoch signifikant ($p < 0.001$) erhöht: 30 ± 6 mm Hg in der Tibialis-anterior-Loge und 14 ± 3 mm Hg in der oberflächlichen hinteren Muskelloge. Die entsprechenden Muskeldrücke bei den Kontrollpersonen waren 24 ± 5 mm Hg bzw. 7 ± 2 mm Hg. In der Klaudikantengruppe könnte die Muskeldrücker-

höhung während der Muskelkontraktionen die Muskeldurchblutung weiterhin reduzieren und die ischämischen Schmerzen verstärken.

Compartment syndromes in the lower extremity are sometimes associated with arterial occlusive disease (4, 5). There are, however, few studies on intramuscular pressure in leg ischemia. Thus, an increased intramuscular pressure was found experimentally following temporary ischemia (8). An elevated intramuscular pressure was also found in patients with intermittent claudication during exercise (7). In the present study intramuscular pressure was determined in 10 patients with intermittent claudication and in 10 normal persons at rest, during and after exercise.

MATERIAL AND METHODS

Patients

Ten patients (5 males and 5 females, aged 52 - 72, mean 63 years) with disabling claudication, not planned for operation, were studied. Walking distance was 256 $\pm$ 162 m, symptoms beginning after 43 $\pm$ 18 m. Blood pressure of the big toe was 48 $\pm$ 10 mm Hg (mean $\pm$ SD) in the most affected leg. Patients with gangrene or pain at rest were not included. The disease was bilateral in all patients but intramuscular pressure was only measured in the most affected leg. The intramuscular pressures of the claudicants were compared with the intramuscular pressures of 10 healthy persons (5 males and 5 females, aged 50 - 73 years).

Intramuscular pressure measurement

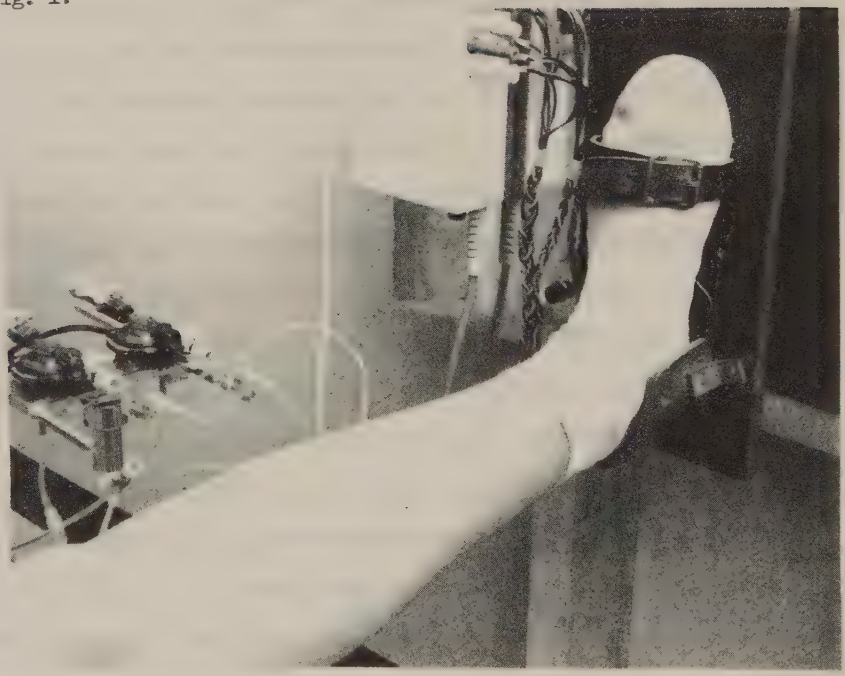
Intramuscular pressure was measured with the wick technique described in detail previously (6). In the wick catheter fibrils protrude from the bore of the catheter to prevent an obstruction of the catheter. The pressures were recorded with an electromagnetic transducer and recorder (Siemens Elema, Sweden). The pressures within the anterior tibial and the superficial posterior compartments were measured at rest with the patient in a sitting position, Fig.1. Intramuscular pressures were then measured at a maximal work load for 7 min or until pain forced the patients to stop. The exercise consisted of isometric activation of dorsiflexors and plantarflexors of the foot every second. The foot was attached to an isometric exerciser and the workload was continuously monitored only to verify that the work was constant during the exercise. After exercise the intramuscular pressure was followed until the pressure had returned to the preexercise level.

RESULTS

Intramuscular pressure at rest and during exercise in 10 patients with intermittent claudication and in 10 normal subjects of the same age is given in the Table. At rest there was no significant difference in intramuscular pressure between claudicants and healthy subjects. During exercise, however, the intramuscular pressures were significantly higher in the claudicant group in both the anterior tibial, 30 ± 6 mm Hg ($p < 0.001$) and the superficial posterior compartment, 14 ± 3 mm Hg ($p < 0.001$), than in the normal subjects, 24 ± 5 mm Hg and 7 ± 2 mm Hg, respectively. The pressures returned to preexercise levels within one

minute in both groups.

Fig. 1.



Experimental set-up for measurement of intramuscular pressure in the lower leg. Wick catheters attached to pressure transducers are placed in anterior tibial and superficial posterior compartments. The foot is attached to an isometric exerciser.

TABLE

Intramuscular pressures (mm Hg) in the anterior tibial and the superficial posterior compartments in 10 patients with intermittent claudication and 10 healthy subjects at rest and during exercise. Values are given as mean ± SD.

	Claudicants	Healthy subjects
Anterior tibial compartment		
At rest	9 ± 2	8 ± 1
At work	30 ± 6	24 ± 5
Superficial posterior compartment		
At rest	5 ± 2	4 ± 3
At work	14 ± 3	7 ± 2

DISCUSSION

The mechanism behind the increased intramuscular pressure during exercise in patients with intermittent claudication may be explained by a damage to the capillary walls due to longstanding ischemia in patients with intermittent claudication. The normal transcapillary movement of fluid into the active muscles known to occur during exercise (2) may be enhanced, leading to an increase of the interstitial fluid as proposed by Reneman (7), who also found increased intramuscular pressure during and after exercise in patients with intermittent claudication. An increase of interstitial fluid is known to raise intramuscular pressure (1). Another explanation of the raised intramuscular pressure in these patients may be swelling of the muscle fibres due to increased lactate formation (3). In the present study the intramuscular pressure was higher in the anterior tibial compartment ($p < 0.001$) than in the superficial posterior compartment both in claudicants and in normals. The reason for this is probably that the walls of the anterior tibial compartment are less elastic than those of the superficial posterior compartment.

In patients with arteriosclerotic occlusive disease the distal blood pressure is reduced. Therefore the tissue blood perfusion will be inadequate even with a relatively mild increase in intramuscular pressure. Thus, the increased intramuscular pressure seen in patients with intermittent claudication during exercise as compared with healthy subjects may contribute to decrease tissue blood perfusion and perhaps aggra-

vate pain. It may be supposed that fasciotomy may be of benefit in the treatment of intermittent claudication.

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INTRAMUSCULAR PRESSURE AFTER REVASCULARIZATION OF THE POPLITEAL ARTERY IN SEVERE ISCHEMIA.

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Abstract

Swelling is known to occur after peripheral revascularization. In the present study of 14 patients undergoing revascularization of the popliteal artery for severe ischemia leg swelling and intramuscular pressure were recorded before and after operation. Calf circumference increased with a maximum swelling of 3.9 $\pm$ 1.1 cm on the 6th postoperative day. There was a gradual increase in intramuscular pressure from 9 $\pm$ 2 mm Hg on the day before operation in the anterior tibial compartment to a maximum pressure on the 6th - 7th postoperative day, 26 $\pm$ 4 mm Hg. Similar intramuscular pressure changes were seen in the superficial posterior compartment. These high intramuscular pressures may lead to a compartment syndrome and perhaps graft failure which was actually observed in one case. Deep-vein thrombosis in the post-operative course may contribute to the high intramuscular pressures. Phlebography revealed a deep-vein thrombosis in 2 patients. In conclusion popliteal revascularization causes leg swelling and increased intramuscular pressure which may lead to a compartment syndrome and graft failure. Therefore follow-up of intramuscular pressure in patients with marked swelling after distal revascularization procedures and early fasciotomy may be considered on wide indications.

Key words: Intramuscular pressure, popliteal revascularization, leg swelling.

Introduction

The patency of arterial by-pass grafts in the early postoperative period is influenced by several factors including adequate arterial run-off and venous outflow.[1, 2] Peripheral vascular procedures frequently produce massive swelling of the lower extremity.[3,4,5] The mechanism of this swelling is not fully understood Postischemic increased capillary permeability [4,5], old postthrombotic changes with venous hypertension and postoperative acute deep-vein thrombosis may be factors, responsible for the edema of arterial reconstruction. [1,2,3] Some authors have suspected the surgical trauma to the lymphatic vessels being the main factor responsible for the edema.[6,7,8] The degree of swelling is correlated to the degree and duration of ischemia. [3] This swelling may initiate a compartment syndrome. [9] In this condition the intramuscular pressure is increased and compromises the circulation within the compartment. Experimental models have also demonstrated significant impairment of blood flow in the presence of high intramuscular pressure. [10,11,12] The importance of relieving fasciotomy in these cases has been stressed by Patman. [13] In his review of 2 000 peripheral arterial reconstructive procedures the frequency of fasciotomy was, however, only 0.45 %. There are no previous studies of lower extremity intramuscular (intracompartmental) pressure following reconstructive peripheral vascular surgery in man. The aim of the present study was to determine intramuscular pressure and the degree of leg swelling before and after revascularization of the popliteal artery in severe ischemia and to evaluate the need of fasciotomy in these cases.

Material and methods

Patient material. Fourteen patients (9 males and 5 females, aged 53 - 91, mean 67 years) planned for a femoropopliteal by-pass procedure were submitted to the study. Indication for operation was limb-threatening ischemia. The patients were preoperatively evaluated with measurement of the distal toe pressure using strain-gauge technique. Systolic blood pressure of the big toe was below 25 mm Hg in the diseased leg, Aortofemoral angiography showed occlusions of the superficial femoral artery with an outflow below the popliteal artery of 1 - 3 arteries patent to the ankle. The following procedures were performed: Eleven femoro-popliteal by-passes below knee, using 6 mm Gore-Tex, 2 femoro-tibial by-passes using a composite graft of 6 mm Goro-Tex and the saphenous vein and 1 femoro-popliteal by-pass above knee, using a 6 mm Gore-Tex graft. Graft patency was ascertained by clinical examinations and ultrasound doppler ankle pressure measurements. In 6 patients phlebography (according to Gullmo)[14] was performed during the postoperative period.

Intramuscular pressure measurement. Intramuscular pressure was measured in the anterior tibial and the superficial posterior compartments of the diseased leg in the supine patient on the day before operation and once every day during 8 postoperative days. In four patients intramuscular pressure was also measured in the two compartments in contralateral, "healthy", leg for comparison. The wick technique described in detail previously was used.[15] In the wick catheter fibrils protrude from the bore of the catheter to prevent an obstruction of the

catheter. The catheter was introduced through a 16-gauge epidural needle in the muscle compartment under superficial local anesthesia. The epidural needle was removed leaving the wick catheter in place. The catheter was filled with sterile heparinized saline. The pressures were recorded with an electromagnetic transducer and recorder (Siemens Elema, Sweden).

Calf circumference was measured prior to intramuscular pressure measurement.

Results

Intramuscular pressure. The intramuscular pressures in 28 compartments of 14 legs in 14 patients before and after popliteal revascularization are seen in Figs. 1 and 2. There was a gradual increase in intramuscular pressure in the anterior tibial compartment from 9 $\pm$ 2 mm Hg on the day prior to operation to a maximum pressure on the 6th - 7th postoperative day, 26 $\pm$ 4 mm Hg. The intramuscular pressures were slightly lower, 24 $\pm$ 4 mm Hg on the 8th postoperative day. The intramuscular pressure in the control leg remained unchanged, 9 $\pm$ 2 mm Hg, during the postoperative period (Fig. 1) The intramuscular pressure in the superficial posterior compartment showed similar changes increasing from 5 $\pm$ 1 mm Hg prior to operation to a maximum of the intramuscular pressure on the 6th - 7 th postoperative day, 15 $\pm$ 4 mm Hg, followed by a slight decrease on the 8th postoperative day, 13 $\pm$ 2 mm Hg. In the contralateral leg, the intra-

muscular pressure was unchanged during the same period of time, 6 ± 1 mm Hg, (Fig. 2). In one patient the intramuscular pressure rose to a maximum pressure of 38 mm Hg in the anterior tibial and 25 mm Hg in the superficial posterior compartment on the 6th post-operative day. The graft occluded and a thrombectomy and fasciotomy was performed. After this procedure the graft was patent at the follow-up after 3 months. Intramuscular pressure measured the day after reoperation was 11 mm Hg. The overall 3 months patency rate was 100 %. Out of 6 postoperative phlebographies performed due to extreme swelling and high intramuscular pressure 2 phlebograms showed the presence of a deep-vein thrombosis, while 4 phlebograms were normal. The two cases with concomitant deep-vein thrombosis had high intramuscular pressures (maximum pressures of 28 mm Hg and 32 mm Hg respectively in the anterior tibial compartment on the 6th postoperative day).

Calf circumference. There was a gradual increase in calf circumference that parallelled the increase in intramuscular pressure, Fig. 3. As can be seen in the figure the maximum increase in calf swelling occurred on the 6th postoperative day, 3.9 ± 1.1 cm.

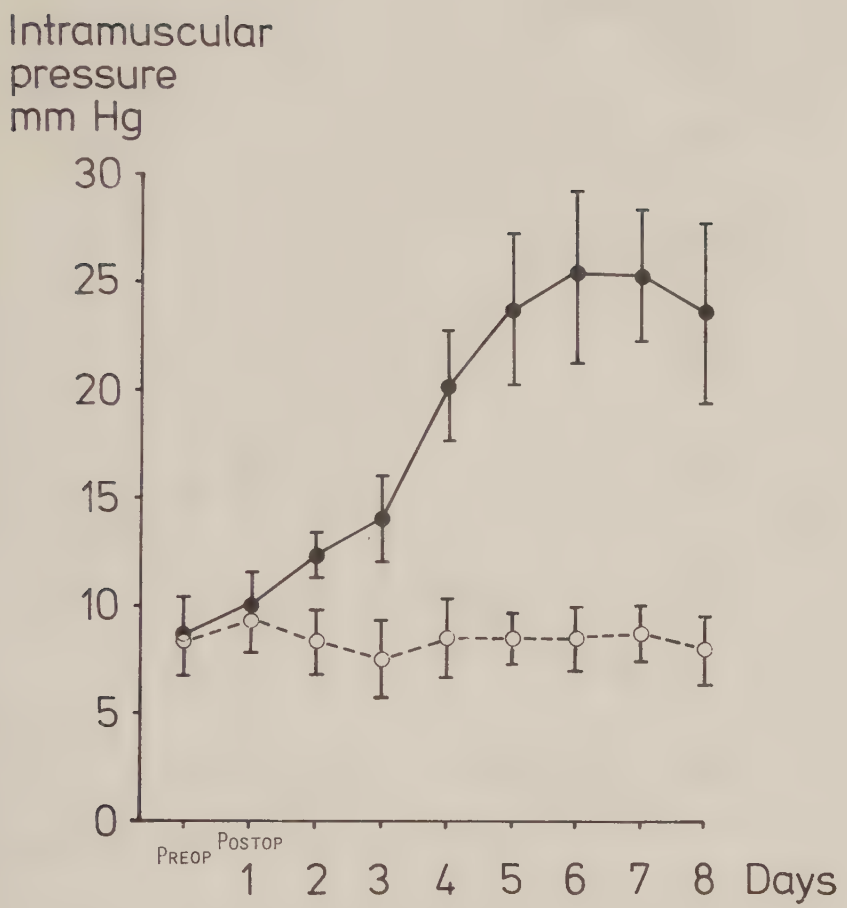

Fig. 1. Intramuscular pressure (mean ± SD) in the anterior tibial compartment before and after popliteal revascularization. ●——● Diseased leg (n = 14) ; o---o control leg (n = 4).

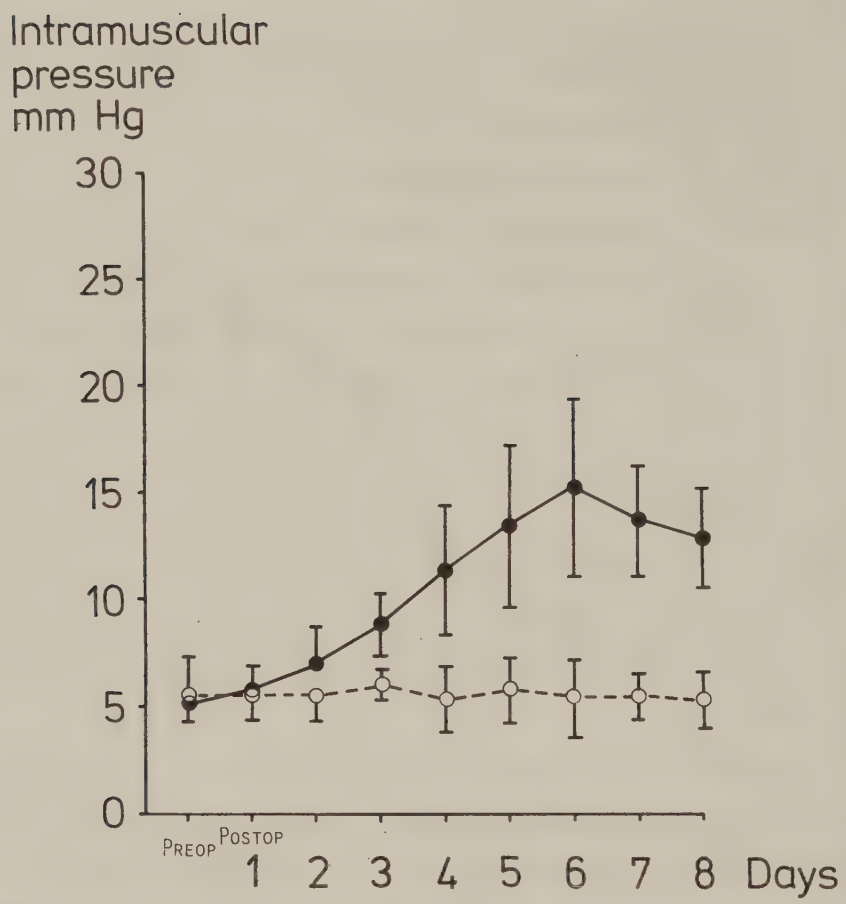

Fig. 2. Intramuscular pressure in the superficial posterior compartment before and after popliteal revascularization (symbols as in Fig. 1.).

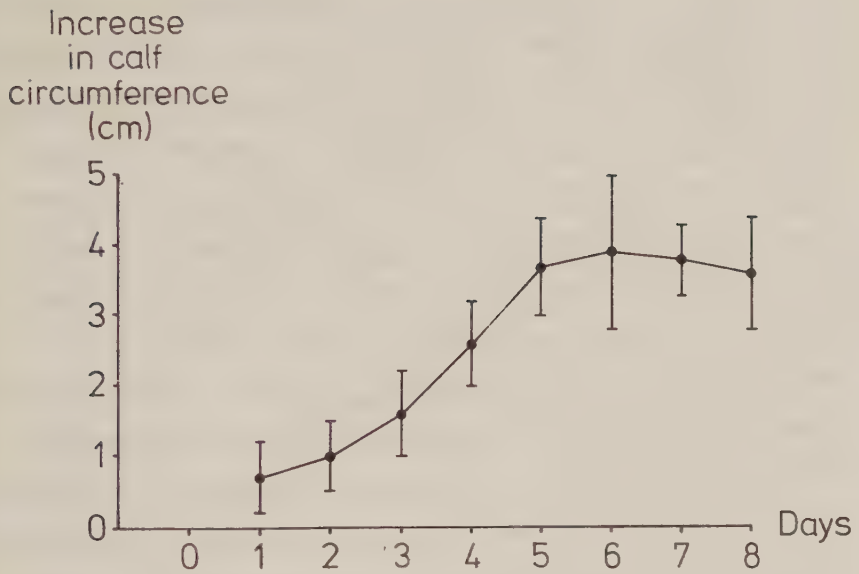

Fig. 3. Increase in calf circumference after popliteal revascularization (n = 14).

Diseussion

The mechanism of the postoperative swelling of the leg following revascularization is not fully understood. A common opinion is that the distal anoxia seen during the period of arterial occlusion causes damage to the capillary walls which leads to an increased capillary permeability. Following a successful femoro-popliteal reconstruction there can be a massive transudation and extravasation of plasma resulting in an increased extravascular fluid and tissue edema.[13] Significant swelling of the tissues within a muscle compartment causes an increased intramuscular pressure.[9] In the present series the degree of leg swelling was correlated to the increased intramuscular pressure with a maximum leg swell-

ing on the 6th postoperative day. One patient developed a compartment syndrome and graft failure on the 6th postoperative day. The intramuscular pressure in this case was 38 mm Hg which is well above the suggested critical pressure level of 30 mm Hg for a compartment syndrome. [16] The postoperative leg swelling may also be due to concomitant venous hypertension or the presence of a deep-vein thrombosis. [1,2] Husni concluded, however, that deep-vein thrombosis can not be considered the primary factor underlying the edema of arterial reconstruction. [3] In the present material 2 out of 6 phlebograms performed, revealed a deep-vein thrombosis. Intramuscular pressure was rather high in the two cases with deep-vein thrombosis. It has previously been shown, that deep-vein thrombosis causes an increased intramuscular pressure.[10] It may be added that a combination of distal revascularization and deep-vein thrombosis may be a risk factor for the development of a compartment syndrome. Interruption of lymphatic channels may also be an important factor in the postoperative swelling. [6,7,8] Fasciotomy following femoro-popliteal by-pass procedures is rare.[13,17] It may be suggested that the risk for the development of a compartment syndrome following such procedures may be underestimated. The anterior tibial compartment is probably most vulnerable because of its tight walls.[17] In the present series intramuscular pressure was higher in this compartment than in the superficial posterior compartment ($p < 0.01$). Patients with arteriosclerotic occlusive disease should be more prone to develop a compartment syndrome since even after revascularization the distal blood pressure is reduced in many cases. Therefore the tissue blood perfusion will be inadequate even with a relatively mild increase in intramuscular pressure. [18]

This study shows that revascularization of the popliteal artery causes swelling of the lower leg and an increased intramuscular pressure which may lead to a compartment syndrome within about one week. A compartment syndrome of the lower leg is considered to occur at an intramuscular pressure above 30 mm Hg, but the pressure level for a compartment syndrome may be lower if the distal blood pressure is lower than normal as in patients with arterial occlusive disease. In order to facilitate arterial and venous run-off and to enhance graft patency, follow-up of intramuscular pressure after reconstructive peripheral vascular surgery, and early fasciotomy in patients with remaining high pressure is suggested. Since fasciotomy has few complications[13] it would be of interest to study the effect of routine fasciotomy in revascularization procedures of the popliteal artery in severe ischemia.

Acknowledgement

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INTRAMUSCULAR PRESSURE CHANGES DURING AND AFTER REVASCULARIZATION OF THE FEMORAL ARTERIES IN MAN

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Abstract

Intramuscular pressures in the anterior tibial compartments of the lower extremity were measured by the wick catheter technique in 5 patients undergoing revascularization of the femoral arteries by bifurcation grafting, because of occlusive artheriosclerotic disease.

The intramuscular pressure at rest was within a normal range preoperatively 9.1 $\pm$ 4.5 mm Hg, but raised significantly to a maximum level 4-6 hours after reestablishing blood flow (22.4 $\pm$ 5.0 mm Hg, followed by a gradual decrease over 5 postoperative days and reached the preoperative value on the 5th postoperative day, 8.7 $\pm$ 5.1 mm Hg. Changes in calf circumferences reflects the changes in intramuscular pressure. No significant changes in intramuscular pressures were seen when measured at different times during the day. An addition of a thoracic epidural anaesthesia did not effect the intramuscular pressures compared to a combination of balanced anaesthesia alone. During occlusion of the aorta (clamping) no changes in intramuscular pressures were seen, but the pressure raised significantly immediately after declamping.

The intramuscular pressures in the anterior tibial compartment correspond well with the findings on metabolic events seen after declamping suggesting an imcomplete ischaemia of the leg muscles with an insufficient tissue perfusion.

During elective and emergency arterial reconstructive procedures the distal circulation may be compromised or intrrupted for a significant duration. Such a condition, e.g. seen during clamping and declamping of the aorta during reconstructive surgery of the aortic bifurcation, induces temporary incomplete ischaemia of the leg muscles (12). This may lead to an increased tissue pressure and will be of particular importance in muscles surrounded by non-compliant fascias as seen in the lower limb compartments and will thus be involved in compartment syndromes.

Theoretical consideration of the factors involved in maintaining vascular equilibrium and experimental evidence in animals and man indicate that at high intramuscular pressures there may be a sharp decline in blood flow even at tissue pressures below mean arterial pressure (2).

No studies have yet been reported on intramuscular pressures in man during arterial vascular reconstructive surgery. By the development of the wick catheter technique for measuring intramuscular pressure (10), it has become possible to perform continuous pressure recordings. Quarfordt et. al. have recently showed that the intramuscular pressure in the lower leg remained nearly unaffected by a short term ischaemia but was slightly increased during the period of reactive hyperemia (13).

The aim of the present study was to define whether intramuscular pressure in the anterior tibial compartment changes or not at clamping and declamping of the aorta in reconstructive surgery for arteriosclerotic

disease of the aortic bifurcation, and to see if revascularization of the femoral arteries results in an increased intramuscular pressure during the early postoperative phase.

Material and methods

Patient material

Five patients, 3 males and 2 females, with disabling thigh and calf claudication were submitted to the study. Average age was 67 years (range 57-72 years). The patients were preoperatively evaluated with angiography and measurements of the distal toe pressures utilizing the strain-gauge technique. Angiography revealed aortic occlusions in 3 patients and severe arteriosclerotic stenosis within the bifurcation area in 2 patients.

All patients were reconstructed with an aortic bifuraction graft to the femoral arteries bilaterally (Microvel^{R}-Double Velour, Meadox Inc Ltd). Every operation included crossclamping of the aorta below the renal arteries with a mean occlusion time of 68 minutes.

Anaesthesia

After a starvation time of 6 hours the patients were premidicated with an intramuscular injection of fentanyl (0.05 mg) and droperidol (2.5 mg) approximately 30 minutes before leaving the ward. All patients were given a combination of balanced anaesthesia with flunitrazepam (Rohyphnol^{R}), fentanyl and pancuronium bromide (Pavulon^{R}). Muscle-

relaxation for orothracheal intubation with a Portex low pressure cuff tube, was achieved by succinyl-choline (approx. 1 mg/kg b.w.). The patients were then connected to a volume-controlled ventilator (Siemens Elema 900) and ventilated with a N_2O/O_2 mixture (FiO_2 0.35).

Three of the patients had an additional anaesthesia with a thoracical epidural catheter by continuous infusion of mepivacaine (20mg/ml). Basic fluids were administrated to give a urinary output of 1 ml/kg b.w./hr. Blood losses were assessed and replaced unit by unit. No heparin was administrated. During the operation the patients were monitored with ECG, intraarterial blood pressure and CVP; diuresis was followed hourly.

Postoperatively Dextran 40 (Rheomacrodex^R) 500 ml/day was administrated during 5 postoperative days. The patients were not extubated immediately postoperatively but allowed to stay on the ventilator until they reached a normal body temperature and had a stable general condition.

Intramuscular muscle pressure measurements

The wick catheter technique was used to measure intramuscular pressure. The catheter was introduced through a 16-gauge epidural needle in the muscle compartment under local anaesthesia. The epidural needle was removed leaving the wick catheter in place. The catheter was filled with sterile heparinized saline. Catheters were placed in the anterior tibial compartments bilaterally on the day prior to operation. The pressures were recorded with an electromagnetic transducer and recorder

(Siemens Elema, Sweden) on the day before operation, immediately pro-operatively, 4-6 hours postoperatively and once every day during 5 postoperative days.

In 3 patients intramuscular pressure measurements also were performed at 3 different times during a day (in the morning, at noon and in the evening) on the 1-3 postoperative days, to evaluate if there were any changes in pressures during the day.

In 3 of the patients intramuscular pressures were additionally recorded in Operating Room after cross-clamping of the aorta, before declamping and immediately after declamping.

At the time for each pressure measurement the calf circumference was measured at a defined, marked site in mid-calf position, All pressure recordings were performed with the patient in a supine position and the zero level was taken on the level of the tip of the catheters. The data were analyzed statistically by means of analysis of variance. Mean values with standard deviations are given in all tables and figures. Significance is expressed as $^{x}(p < 0.05)$, $^{xx}(p < 0.01)$ and $^{xxx}(p<0.001)$.

Results

The pressures in 10 compartments of 5 patients undergoing bifurcation grafting procedures for femoral revascularization because of arterio-sclerotic occlusive disease were measured.

The compartment pressures in the anterior tibial compartments preoperatively, 4-6 hours after reestablishing blood flow to the lower limbs and during 5 postoperative days are shown in Fig. 1. A statistically significant increase of intramuscular pressure is seen when comparing preoperative values with pressure values immediately postoperatively (9.1 ± 4.5 mm Hg vs. 22.4 ± 5.0 mm Hg), followed by a gradual decrease of the intramuscular pressures over the early postoperative period. An almost normalization of the pressure was seen on the 5th postoperative day (8.7 ± 5.1 mm Hg).

By comparing the intramuscular pressures recorded in patients anaesthesized with a combination of a balanced anaesthesia and patients who had an additional thoracic epidural anaesthesia no statistically significant differences were observed. (Table 1.)

No statistically significant variations over the day were observed in those patients where intramuscular pressures were measured at different hours of the day, (Fig. 2.)

The intramuscular pressures in 6 compartments were recorded during the cross-clamping of the aorta and following declamping. The pressures at different sequences of the operative procedure in the anterior tibial compartment are shown in Fig. 3. No raise in pressure is noticed during the cross-clamping but a significantly rapid increase in intramuscular pressure is observed during the post-ischaemic phase

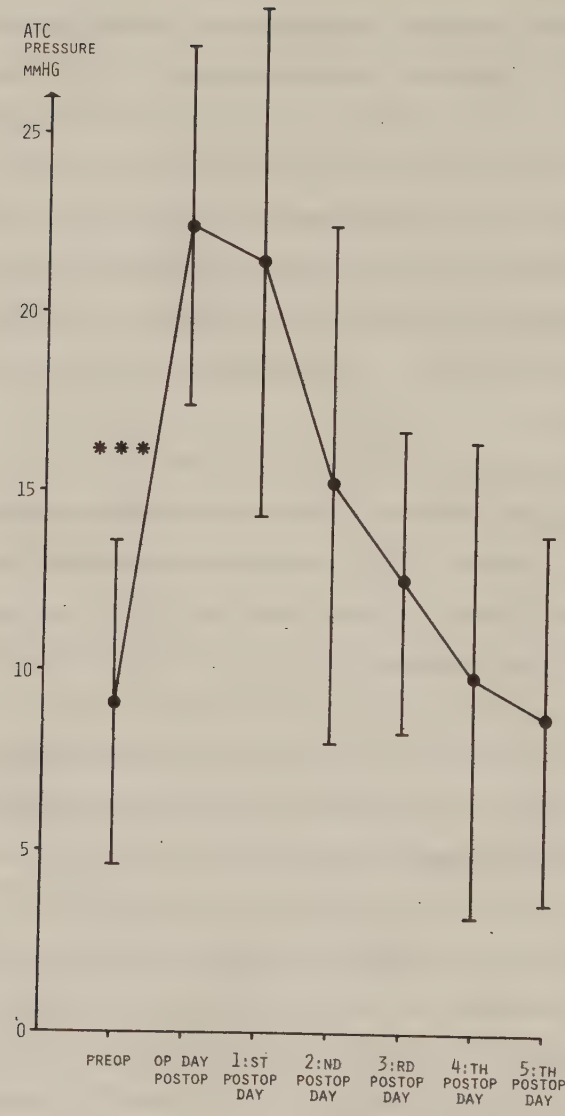

Fig. 1. Intramuscular pressure changes in anterior tibial compartment (ATC) after revascularization of the femoral arteries in man (mean ± SD, n = 10).

Table 1

Intramuscular pressures at rest, in the anterior tibial compartment, prior to and after revascularization of the femoral arteries comparing two anaesthetic methods, Gr A, a combination of anaesthesia + a thoracic epidural anaesthesia, and Gr B, a combination of balanced anaesthesia alone, (mean ± SD, mm Hg).

	Group A (n=6)	Group B (n=4)	p
Preoperatively	12.6 ± 3.5	12.8 ± 3.1	n.s
Postoperatively	21.6 ± 3.4	23.5 ± 6.7	n.s
Postoperative day 2	21.8 ± 5.3	20.3 ± 6.7	n.s
Postoperative day 5	12.0 ± 4.5	12.8 ± 2.7	n.s

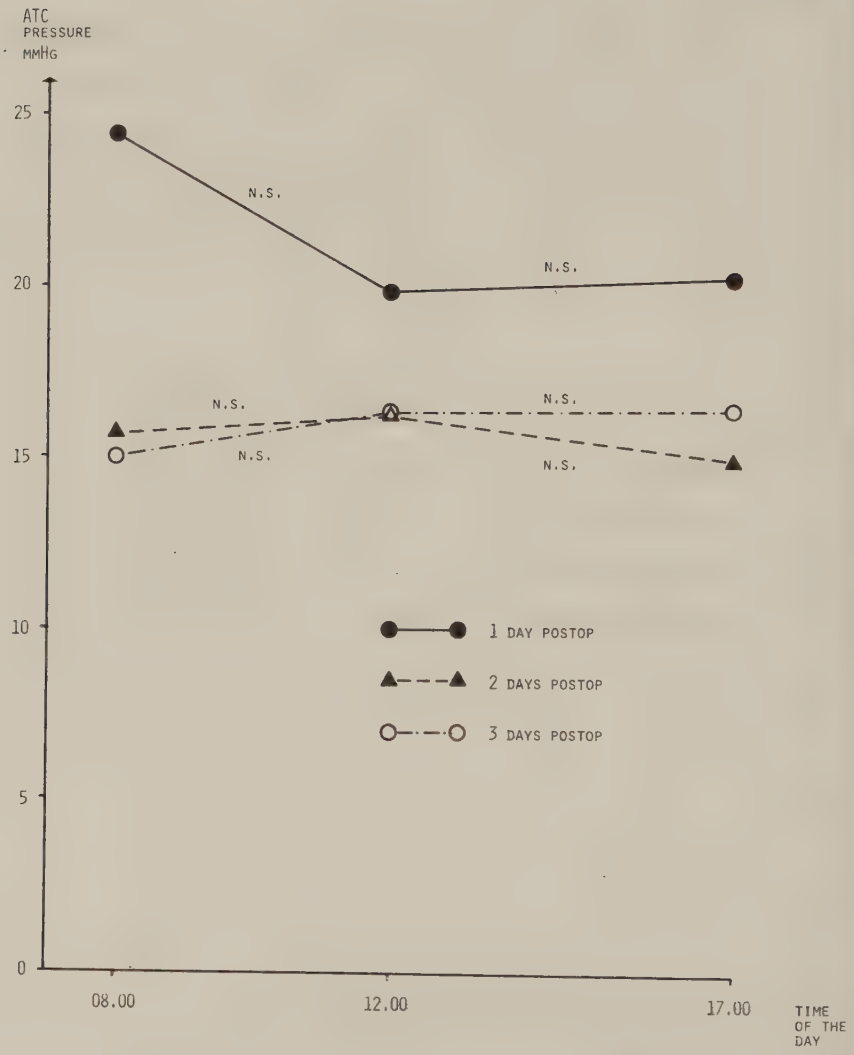

Fig. 2. Intramuscular pressures in the anterior tibial compartment (ATC) at different time of the day, measured on the 1st, 2nd and 3rd postoperative day (mean ± SD).

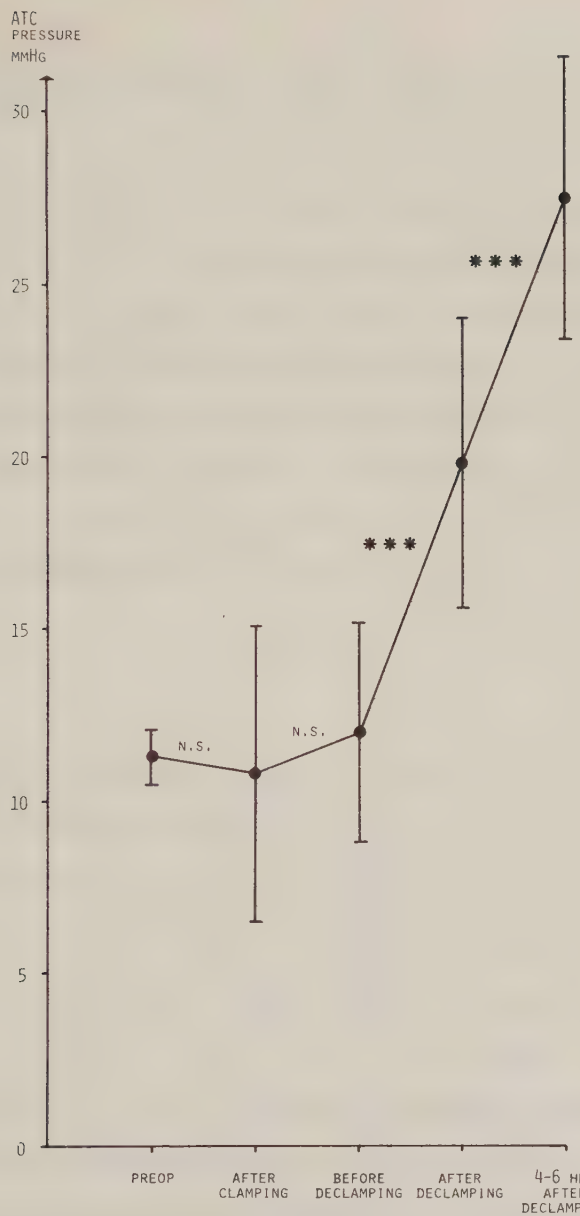

Fig. 3. The intramuscular pressure changes in the anterior tibial compartment during and after occlusion of the abdominal aorta (mean ± SD).

followed declamping of the aorta. A maximum pressure level seems to be reached 4-6 hours after declamping.

Changes in the circumference of the calf correspond well with the recorded changes in intramuscular pressure (Fig. 4). To be stressed is that no significant changes in systemic arterial blood pressure were seen during the operation nor postoperatively in the patients. Approximately 6 weeks postoperatively the distal blood pressure of the big toe had increased significantly by an average 27.5 mm Hg compared with pressures obtained preoperatively (32 ± 18 mm Hg vs. 60 ± 24 mm Hg ($p < 0.01$). At this time all patients also had a complete relief of symptoms subjectively.

Discussion

A temporary cross-clamping of the aorta during aortic reconstructive surgery has been shown to induce incomplete ischaemia of the legs. Only minor skeletal muscle metabolic events occur during aortic clamping. However, after aortic declamping, when the blood flow is restored in the legs, a severe metabolic derangement with loss of high-energy phosphate compounds has been observed, indicating a dysfunction or damage of the muscle cells (1. 14). Eklöf et. al. have shown that during clamping the muscle lactate/pyruvate ratio increased while intramuscular pH and femoral venous blood flow decreased, indicating insufficient tissue perfusion. Energy charge (EC), the adenylate (ATP+ADP+AMP) and creatine (PCr + Cr) pools were unchanged. After restoration of the

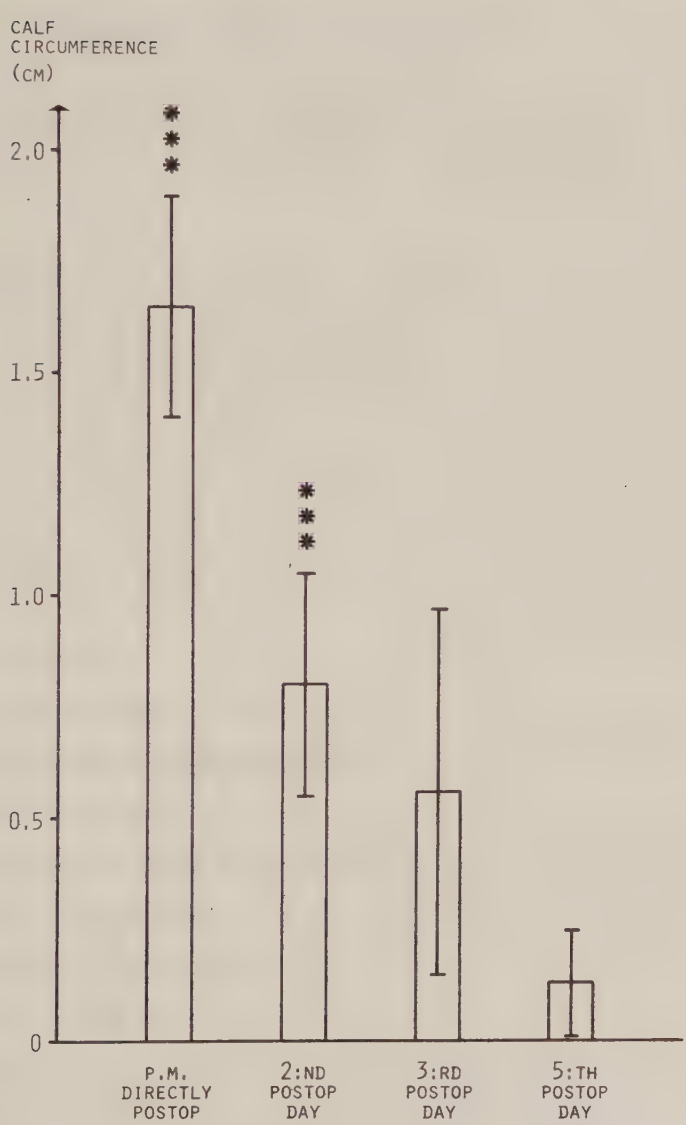

Fig. 4. Changes in calf circumferences (cm) at different times postoperatively compared with preoperative values (mean ± SD).

blood flow extreme metabolic and morphological changes in the muscle tissue were observed. The adenylate and creatine pools declined approximetely 30 per cent and the energy charge of the adenine nucleotides dropped significantly (4).

The metabolic pool changes were closely related to the changes in the lactate/pyruvate ratios. Morphological signs of membrane disturbances such as fibre edema and swelling of mitochondria, were seen in many muscle fibres after declamping (14). Jennings & Ganote have shown that 40 minutes after incomplete myocardial ischaemia reperfusion causes a massive and sudden extensive cell swelling, rupture and loss of mitochondria (8). However, only 1-3 per cent of the muscle fibres seem to be irreversibly injured (12).

This corresponds well with our findings of a gradual decrease in intramuscular pressure towards a complete normalization on the 5th postoperative day. Available evidence indicates also, that whatever the cause of the raised i.m. pressure, blood flow will be decreased and may even temporarily cease altogether as a result of a combination of active arteriolar closure and passive capillary compression. The degree of arteriolar closure will depend on the level of vasomotor tone at a given tissue pressure and intravascular pressure, while the amount of capillary compression will depend on the height of the total tissue pressure immediately surrounding the capillaries (2,5,15). However, the modern concept is that the raised inramuscular pressure is secon-

dary to an abnormally increased extravascular hyperosmolarity (6,9).

Since capillary filtration equilibrium occurs at 13 mm Hg at the anatomical site of postcapillary venules, net fluid filtration occurs into the tissues from the precapillary and capillary vessels, while net fluid absorption back into the blood occurs in the postcapillary venules where the blood pressure is less than 13 mm Hg. On the other hand fluid return via terminal lymphatic vessels is also of importance to remove excess extracellular fluid via normal and slightly edematous muscle. However, lymphatic return of edema fluid will be constrained when the tissue-fluid pressure is high enough for the lymphatic vessels to be occluded (7). Since capillary blood pressure in 5-10 micrometer-diameter vessels is approximately 20-30 mm Hg tissue-fluid pressure greater than 30 mm Hg is postulated to reduce capillary blood flow by microvascular occlusion. Furthermore muscle ischaemia significantly raises capillary membrane permeability to plasma proteins (3).

The used method for measuring intramuscular pressures records actually the total tissue pressure which means that the obtained pressures reflect both interstitial pressure and pressure raise due to swelling of the cells themselves.

As earlier stated by Qvarfordt et. al. the wick catheter technique is a convenient method for measuring intramuscular pressures when continuous recordings are demanded (13).

In the present investigation it was found that intramuscular pressure is almost unaffected during cross-clamping of the aorta, followed by a significant increase of pressure after restoration of blood flow which corresponds well with the earlier described events on muscle metabolism and morphological derangements seen after incomplete temporary muscle ischaemia (11).

Our findings also correspond well with earlier reports of just a small amount of irreversibly injured muscle fibres, because of the almost complete normalization of the intramuscular pressures postoperatively. No variations in intramuscular pressures were seen at different times during a 24 hour period. The changes in calf circumferences reflect well the changes in intramuscular pressure.

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THE INFLUENCE OF INCREASED INTRAMUSCULAR PRESSURE ON PLATELET ADHESION IN PTFE GRAFTS IN VIVO. AN EXPERIMENTAL MODEL.

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Key words: Intramuscular pressure, In-111-oxine, platelet adhesion, arterial grafts.

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Abstract

Thrombogenicity of the graft material and technical errors are factors involved in early graft failure in small diameter grafts. The frequently seen postoperative swelling of the leg may cause an increased intramuscular pressure and early graft failure. Using a pig model, the present in vivo investigation demonstrated that an increased intramuscular pressure of 30 mmHg or more by means of a blood pressure cuff around the calf significantly increased the amount of platelets that adhered onto PFTE grafts. 111-Indium-labeled autologous platelets and gamma camera scintigraphy was employed. Intramuscular pressure was measured with the wick technique. The results emphasize the need for the follow-up of intramuscular pressure after lower limb vascular revascularizations with grafts and fasciotomy is recommended at pressures of approximately 30 mm Hg.

Introduction

Usually poor results are encountered with small diameter arterial grafts, with a diameter less than 6 mm, especially when used in conditions of high resistance and low flow, e.g. in the lower extremity (4, 11, 20).

An adequate blood flow is fundamental for a good outcome. Factors reported to be involved in early graft failure are thrombogenicity of the graft material (6, 19) and technical errors (5).

The introduction of ^{111}In-oxine as a platelet label has added new dimensions to the study of platelet kinetics, because it enables the use of gamma nuclear imaging technique, suitable for in vivo studies of graft thrombogenicity (3).

Another wellknown phenomena seen in peripheral vascular reconstructive surgery e.g. femoro-popliteal by pass B.K., is the postoperative swelling of the calf, due to edema (16). This swelling leads to an increased intramuscular pressure which may lead to an acute compartment syndrome, affecting the blood flow (1). An increased intramuscular pressure may therefore be a third factor of importance in small diameter vascular graft failure, due to a decrease in blood flow which according to previous reports increases the interaction between platelets and grafts surface (3).

It has recently been reported that the critical intramuscular pressure level for a compartment syndrome is 30 mmHg in a canine model. At this pressure level muscle compliance falls sharply. This critical pressure

probably represents a limit to which the fascial sheath can be stretched.

Beyond that limit ischemic necrosis will be imminent (12).

Thus, an increased intramuscular pressure above a certain level could jeopardize the reconstruction performed. By the development of the wick catheter technique for measuring intramuscular pressure, it has become possible to perform continous pressure recordings (14).

The aim of the present investigation was to study the relationship between intramuscular pressure and platelet-graft-surface interaction at different pressure levels.

Material and methods

Six pigs weighing 25-30 kg were anesthetized with intravenous injected Sodiumpentobarbitol (60 mg/kg) and anesthesia was maintained with intermittent injection of the same drug whenever needed. The pigs were intubated and respiration was maintained with a ventilator. No heparinization was employed but fluid (normal saline) was infused intravenously during the experiment.

Graft implantation

Using sterile techniques both femoral arteries were exposed. PTFE (polytetrafluoroethylene) grafts (Gore-Tex^{R}), 4 mm internal diameter and 5 cm long, were implanted in the femoral circulation using end-to-end anastomoses with interrupted 6-0 prolene sutures (superficial

femoral artery). The wounds were not sutured but kept under sterile covering.

Cell separation and labeling procedure during surgery

Four venous blood samples of 15 ml each was withdrawn from the animal, through a venous catheter placed in the jugular vein, into plastic syringes containing 3 ml ACD-NIHA sol. (4.0 g citric acid (monohydrate) 11.0 g sodium citras aup SLS, Glucosahr 11.2 g, Aqua ster. 500 ml) each and mixed gently during and after collection. The blood was transferred into closed sterile glass vials (20 ml) for cellseparation. The vials were centrifuged for 17 minutes at 130 x g (800 rpm) in a balanced clinical bench centrifuge and the supernatant, the platelet-rich plasma (PRP), was removed with the aid of 10 ml syringes with spinal needles and placed into a new vial. pH was adjusted to 6.5 by adding ACD-NIHA sol. and 0.4 ml of 25% human serum albumin (HSA) was carefully layered under the PRP using a 2½ inch long needle. After centrifugation at 500 x g (2 000 rpm) for 12 minutes platelet-poor plasma (PPP) was removed and saved, leaving a platelet layer overlaying the HSA. Following adding of 1 ml PBS (phosphate-buffered saline, pH 7.4, 0.82% NaCl, 0.16 Na_2HPO_4, 0.02 $NaH_2PO_4.2H_2O$), the platelets were easily resuspended by gentle agitation. 111-Indium-oxinate (Byk-Mallinckrodt, Petten, Netherlands), made ready by adding 0.4 ml sterile TRIS buffer (0.2 M, pH 8,0) was added to the cells. The cells were then incubated in a waterbath at 37°C for 20 minutes. The labeled platelets were resuspended in 2 ml PPP and 0.4 ml HSA was

layered under the cells as described above. After centrifugation at 500 x g for 12 minutes supernatant PPP was removed and saved for determination of labeling efficiency, leaving a platelet layer over the HSA. 10 ml "fresh" PPP was added and the platelets were easily resuspended.

The amount of radioactivity in the supernatant and the labeled platelets were determined in a radioisotope dose calibrator and the labeling efficiency (LE) was calculated by the formula LE% =

$$\frac{\text{cellactivity}}{\text{cellactivity + activity in supernatant}} \times 100$$

Platelet function was determined by aggregation test utilizing ADP as stimuli.

Intramuscular pressure measurement

The wick catheter technique was used to measure intramuscular pressure (17). The catheter was placed in the muscle compartment of the calf, bilaterally, utilizing a 16-gauge epidural needle. The catheters were filled with sterile heparinized saline. The pressures were recorded with an electromagnetic transducer and recorder (Siemens Elema, Sweden) during the experiment.

The experimental protocol

The pig was placed in supine position. After the grafts were in place, but before they were exposed to blood, the ^{111}In-labeled

platelets were reinfused intravenously. Ten to fifteen minutes later, blood flow through the grafts was re-established. Blood flows were measured continously with noncannulating Nycotron electromagnetic square wave flowmeters.

As soon as hemostasis was obtained, the pigs were imaged in the supine position. Sequential 600 sec.scintillation camera (Pho Gamma III HP camera, Siemens) images of the graft area were taken and stored in a computer (Gamma 11, Digital Corp). A medium energy parallelhole collimator was used. An energy window was selected over the photon energy 245 keV. The digital images were used to quantitate counts per pixel in several Regions of interest, e.g. the graft (excluding the 2 anastomoses), host artery distal and proximal to the anastomoses, and adjacent soft tissue (average of 3 regions) were selected in the digital images to quantify the ^{111}In activity. From these numbers platelet deposition onto the graft was calculated in the form of an "activity ratio", defined as; (countrate in graft area - countrate in artery area)/countrate in soft tissue area. A ratio greater than zero will then indicate a net platelet deposition onto the graft surface.

One graft served as control while the other graft was the experimental graft (Fig. 1.) Ninety minutes after re-establishing of blood flow through the grafts, the intramuscular pressure on the test-side was raised to approximately 30 mm Hg by external compression of the calf utilizing a blood pressure cuff.

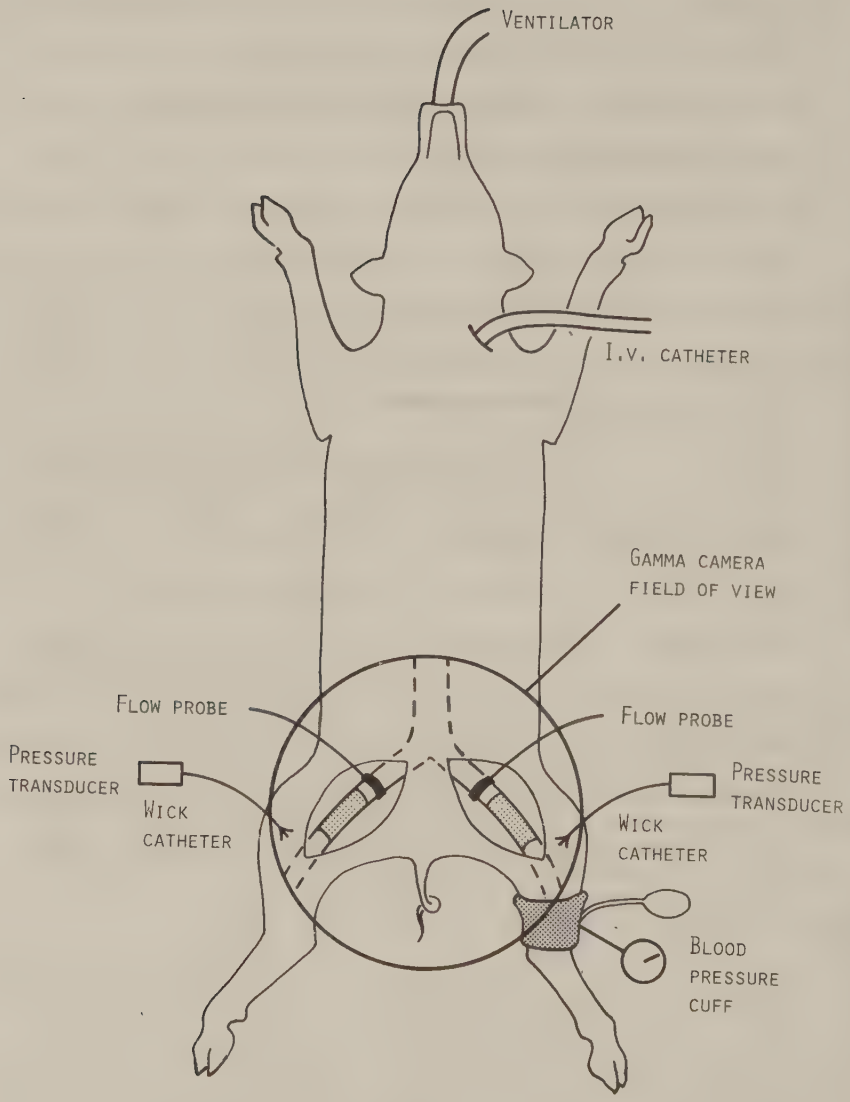

Fig. 1. Schematically - the experimental set-up.

After another 60 minutes the intramuscular pressure was once again raised this time to approximately 60 mm Hg. Platelet uptake was recorded for another 60 minutes.

At the end of the experiment the grafts were isolated, removed and rinsed in saline, and their activities were measured in a well counter (Selektronic) using an energy window including both the 171 and 245 keV full energy peaks. These values were compared to the in vivo values obtained with the scintillation camera. The data were analysed statistically by means of analysis of variance. Mean values with standard deviations are given in all figures. Significance is expressed as *($p<0.05$), **($p<0.01$) and ***($p<0.001$).

Results

The platelets were labeled with an average labeling efficiency of 86 $\pm$ 7 % (mean $\pm$ S.D.). The injected activity was 20.1 $\pm$ 2.8 MBq. Satisfactory aggregation occured in all cases, ten out of the 12 implanted grafts remained patent and form the basis of this report. One graft occluded immediately and was excluded from this study. Another graft, in the test group became occluded after the first increase of the intramuscular pressure and is discussed separately.

Control extremity

All grafts were visible immediately. The activity ratios rapidly increased to a maximum, and then decreased more slowly. Maximum was

reached 60 minutes after re-establishing blood flow through the grafts (4.1 ± 0.7, n=11). Blood flows were approximately constant throughout the experiment (21 ± 7 ml/min) as well as the intramuscular pressure (8.5 ± 4.2 mmHg). (Fig. 2.)

Test extremity

All grafts in the test extremity were also visible immediately as in the control extremity. The activity ratios followed the same curve as shown in the control graft. The same was true concerning blood flow and intramuscular pressures during the first 80 minutes of the experiment. When the intramuscular pressure was increased the activity ratio also increased (3.2 ± 0.5, n=5 v.s. 4.6 ± 0.8, n=5; $p<0.01$) and continued to raise to a maximum of 6.0 ± 0.8 40 minutes later, where it seemed to level out. During the same period of time blood flow decreased with 12 % of the initial flow.

One graft had an even higher increase of activity ratios and was found to be occluded 30 minutes after intramuscular pressure was increased. The activity ratio reached a plateau of approx. 8.6. After the second increase of intramuscular pressure at 150 minutes post declamping activity ratios continued to increase and reached a maximum level of 7.6 ± 0.6 after 30 minutes, indicating a continued platelet deposition. Blood flow was decreased during this second phase with approximately 20 % of the initial and compared to blood flow in the control leg. (Fig. 2.)

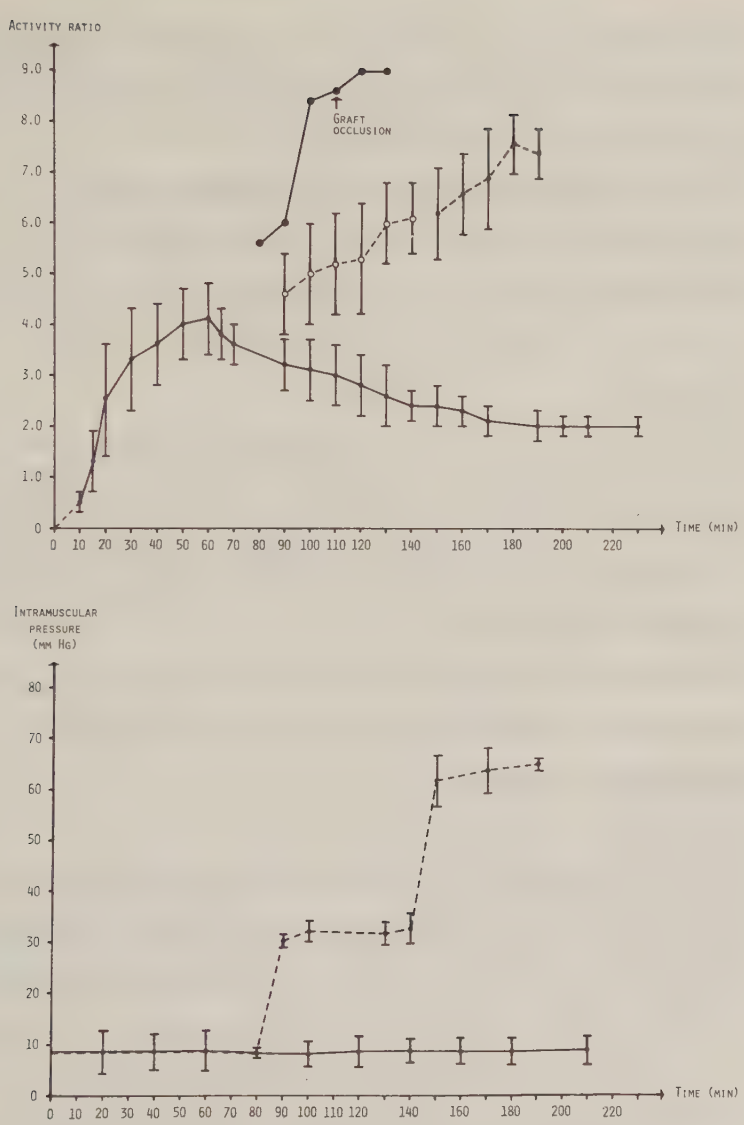

Fig. 2. Activity ratios v.s. time in PTFE grafts, control and test grafts, mean ± S.D. (top)
Intramuscular pressures v.s. time, means ± S.D. (bottom)
control grafts *test grafts*

The difference between test and control grafts as they appeared on gamma camera images during the two periods of increased intramuscular pressure is shown in Fig. 3.

In vitro counts of the grafts showed differences similar to that of activity ratios calculated from the nuclear images (3.6 v.s. 3.7 times higher activity in the test grafts v.s. control grafts).

Discussion

Graft-thrombosis is common following distal reconstructions with small diameter grafts. The reaction of platelets to the foreign graft-surface is an integral part of this process. A complete study of platelet-surface-interactions is central to an understanding of the overall mechanism of graft-thrombosis.

Evans and Irvine demonstrated a direct relationship between platelet adhesiveness and graft failure in Dacron grafts implanted in the femoropopliteal region (7).

From in vitro and ex vivo studies (8, 9) it was recognized that platelet-surface-interactions are sensitive to the velocity of blood. Christenson et.al. have also showed, in a canine model utilizing 111-Indium-labeled platelets, that platelet deposition to PTFE-grafts is a sensitive function of blood flow. Significantly more platelets were deposited onto the graft surface when blood flow was 60 ml/min or less (3). In a recent review, Callow pointed out the fact that small (<6 mm) diameter grafts do not perform well in high resistance

locations or when blood flow is low (2).

Using ^{111}In-oxine to label the platelets enables us to follow the kinetics of platelet deposition. The patterns we have observed (Fig. 2.) could be seen only if labeled platelets were already present in the circulation at the time flow was re-established in the graft. The slope of the curve activity versus time suggests two processes: one resulting in adhesion of the platelets and another contributing to the removal of platelets from the surface.

A wellknown observed fact, to all vascular surgeons, is the post-operative swelling that occurs within the calf in patients reconstructed with distal by-passes (16). This swelling may cause an increased intramuscular pressure (15). In a previous study in patients undergoing femoro-popliteal by pass reconstructions the degree of leg swelling was correlated to the increased intramuscular pressure with a maximum swelling and intramuscular pressure on the 6th postoperative day (18). Available evidence indicates that whatever the cause of the raised intramuscular pressure, blood flow will be decreased and may even temporarily cease altogheter(2, 10, 21). Since capillary blood pressure is approximately 20-30 mmHg, tissue-fluid pressure greater than 30 mmHg is postulated to reduce capillary blood flow by microvascular occlusion (12). These findings correspond well with our results. An increased intramuscular pressure over 30 mmHg resulted in a slight drop in blood flow and a significant increase of the amount of platelets deposited onto the graft surface. In one case a graft

occlusion occured, probably due to a rapid increase in platelet deposition onto the surface. In the present study a raised intramuscular pressure was obtained by using a blood pressure cuff around the calf. The method of applying external pressure on the extremity to create a compartment syndrome has earlier been described (13). The wick technique for measuring intramuscular pressure in this investigation was convenient, since continuous recordings were possible throughout the whole experiments.

The data, obtained from the present study, supports the opinion that an increased intramuscular pressure to approximately 30 mmHg may lead to a compartment syndrome and perhaps early graft failure. In order to enhance graft patency, after reconstructive peripheral vascular surgery, early fasciotomy in patients with pressures exceeding 30 mmHg is suggested.

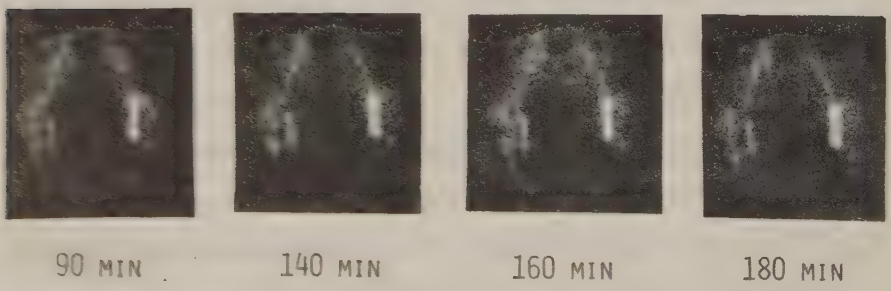

Fig. 3. Computer generated images of femoral arterial PTFE grafts showing changes in platelet deposition with time. The pig's head is up. Right graft - increased intramuscular pressure, left graft control.

Acknowledgements

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INTRAMUSCULAR PRESSURE, VENOUS FUNCTION AND MUSCLE BLOOD FLOW IN PATIENTS WITH LYMPHEDEMA OF THE LEG

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Key words: Intramuscular pressure, venous emptying,
muscle blood flow, lymphedema.

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Summary

Intramuscular pressure, muscle blood flow and venous emptying was studied in seven patients with unilateral lymphedema of the leg. Intramuscular pressure was measured with the wick technique. Muscle blood flow was assessed by means of the ^{133}Xenon clearance technique. Venous emptying was studied with strain-gauge technique. Intramuscular pressure in the anterior tibial compartment of the edematous leg was 30 ± 14 mm Hg at rest, rising to 49 ± 16 mm Hg during exercise ($p < 0.05$). In the healthy leg the pressure rose from 16 ± 8 mm Hg at rest to 28 ± 6 mm Hg during exercise ($p < 0.05$). In the deep posterior compartment similar pressure values were obtained. Muscle blood flow during exercise was significantly higher ($p < 0.05$) in the healthy leg, 32.4 ± 6.8 ml x min^{-1} x (100 g)$^{-1}$ than in the edematous leg. 29.9 ± 4.8 ml x min^{-1} x (100 g)$^{-1}$. Venous emptying was significantly lower ($p < 0.05$) in the diseased leg, 44.7 ± 18.7 ml x min^{-1} x (100 g)$^{-1}$ than in the healthy leg, 61.4 ± 18.9 ml x min^{-1} x (100 g)$^{-1}$. Thus, lymphatic obstruction of the leg causes edema which leads to an increased intramuscular pressure and a decreased muscle blood flow and venous emptying.

Introduction

Compartment syndromes in the lower extremity are often associated with leg edema (1). It has previously been shown that leg edema of venous origin causes an increased intramuscular pressure and a decreased muscle blood flow (2), Fluid return via lymphatic vessels is probably important for removing excess extracellular fluid in muscle since lymphatic obstruction causes edema of the leg (3). The present study was undertaken in order to evaluate the effect of leg edema of lymphatic origin on intramuscular pressure, venous function and muscle blood flow.

Material

Seven patients, five females and two males, aged 46-72 (mean 57) years with unilateral lymphedema of the leg were studied. The left leg was affected in three cases, the right leg in four cases. The lymphedema was secondary to exstirpation of lymph nodes and radiation therapy in the treatment of malignant melanoma in six patients. In one patient the lymphedema was essential. The duration of lymphedema was 31 ± 22 months. The leg swelling was considerable with an increase in calf circumference of 5.2 ± 1.5 cm in the sick leg as compared with the contralateral leg. The patients had moderate pain in the leg on exhaustion. No other treatment than elastic stockings was used.

Methods

Intramuscular pressure measurement was performed with the wick technique described in detail previously (4). The wick catheters were placed

into the anterior tibial and the deep posterior compartments under local anesthesia at the same level about 15 cm below the knee joint. In the wick catheter fibrils protrude from the bore of the catheter to prevent an obstruction of the catheter. The pressures were recorded with an electromagnetic transducer and recorder (Siemens Elema, Sweden). The compartment pressures were measured in the lymphedematous and the contralateral leg at rest with the patient in a standing position. Compartment pressures were then measured during heel-raising every second for at least 5 min (Fig. 1).

Venous emptying was estimated according to Hallböök (5). A tourniquet applied around the thigh was pumped up to 50 mm Hg. The calf volume was registered with strain-gauge technique. When no further increase of calf volume was noted the tourniquet was released and the venous outflow measured. Values below 40 ml x min^{-1} x $(100\ g)^{-1}$ were regarded as subnormal (5).

Systolic pressure of the big toe was measured with a strain-gauge technique to evaluate any arterial disease.

Muscle blood flow was measured in the anterior tibial muscles bilaterally using the ^{133}Xenon clearance technique. The legs were studied one after the other. Approximately 3.5 MBq ^{133}Xenon in 0.1 ml of isotonic saline was injected into the anterior tibial muscles about 15 cm below the knee joint at a depth of about 2 cm using a needle with 0.4 mm

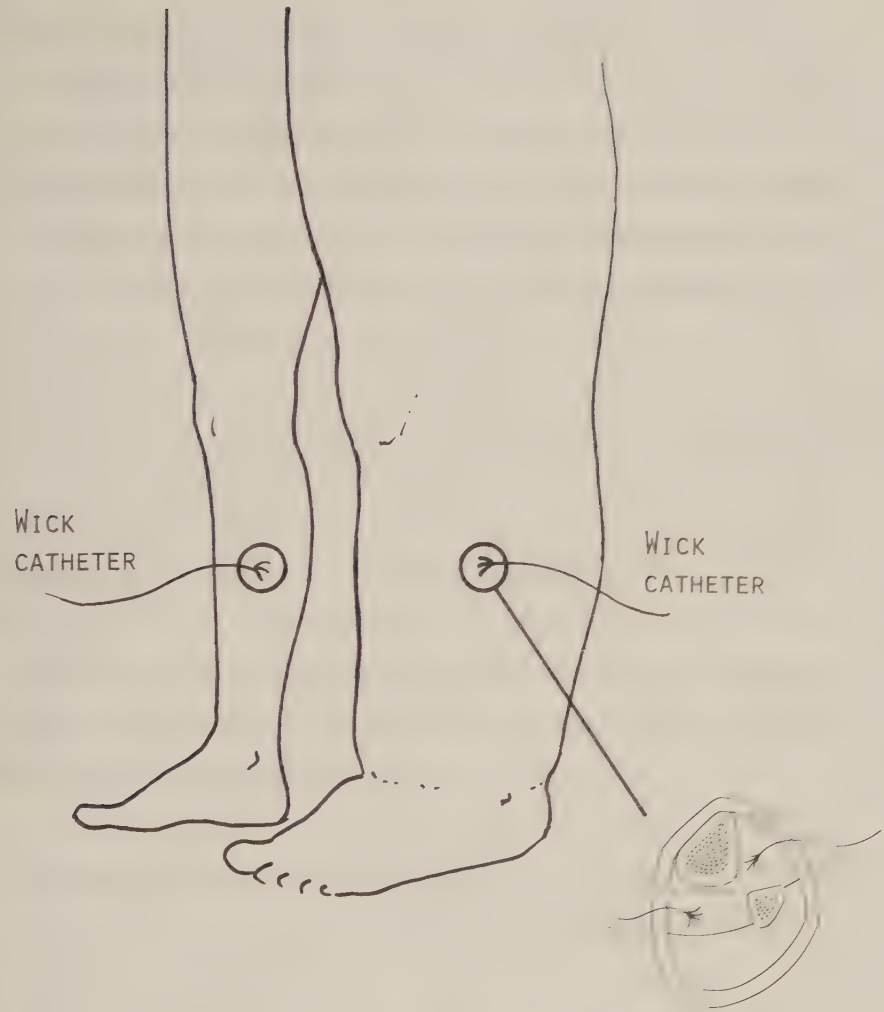

Fig. 1. Intramuscular pressure measurement with the wick technique in both legs in unilateral lymphedema. Inset: wick catheters placed in anterior tibial and deep posterior compartments.

outer diameter, The isotope was slowly injected during 15 sec and the needle was withdrawn 15 sec thereafter. Records were taken from both legs with the patient at rest in a standing position, during heel-raising 60 times per min for 5 min and after exercise. Counting rate was recorded directly over the site of injection with a collimated cadmium telluride detector (TE 101, Pharmacia Electronics, Denmark) attached to the skin surface of the legs with adhesive tape. The detector was connected to a portable memory, Memolog-500 (Pharmacia Electronics, Denmark) working as multiscaler giving digital information of the counting rate variation in 8 sec intervals which after each study was written directly into a computer (ABC 80). The blood flow (f) was calculated from the half-time (T1/2) of the disappearance of the isotope according to the following formula: $f = \frac{\ln 2 \cdot \lambda \cdot 60 \cdot 100}{T\ 1/2}$, where λ represents the partition coefficient for ^{133}Xenon between tissue and blood. A standardized value of 0.7 ul/g was used for λ, since it has been used previously for muscle tissue (6). The calculated muscle blood flow is expressed as ml x min^{-1} x $(100\ g)^{-1}$ tissue. Muscle blood flow was calculated from the decrease in counting rate during the last 2-3 min of the exercise.

Results

Intramuscular pressure in the anterior tibial compartment of the edematous leg was 30 $\pm$ 14 mm Hg at rest, rising to 49 $\pm$ 16 mm Hg during exercise ($p < 0.05$). In the healthy leg the pressure rose from 16 $\pm$ 8 mm Hg at rest to 28 $\pm$ 6 mm Hg during exercise ($p < 0.05$). In the

deep posterior compartment of the diseased leg the intramuscular pressure was 29 ± 8 mm Hg at rest, rising to 45 ± 16 mm Hg during exercise ($p < 0.05$). The corresponding pressure values for the healthy leg was 20 ± 7 mm Hg and 35 ± 19 mm Hg ($p < 0.05$), respectively. The intramuscular pressures were significantly ($p < 0.01$) higher in the diseased than in the healthy leg both at rest and during exercise (Fig. 2).

Venous emptying was significantly lower ($p < 0.05$) in the diseased leg, 44.7 ± 18.7 ml x min^{-1} x $(100\ g)^{-1}$ than in the healthy leg, 61.4 ± 18.9 ml x min^{-1} x $(100\ g)^{-1}$, (Fig. 3). In two edematous legs venous emptying was markedly below 40 ml x min^{-1} x $(100\ g)^{-1}$.

Systolic pressure of the big toe was normal in both the diseased and the contralateral leg. No significant difference in distal pressure was found between the legs.

Muscle blood flow as determined with the ^{133}Xenon clearance technique did not differ significantly between the leg with lymphedema, 2.9 ± 0.9 ml x min^{-1} $(100\ g)^{-1}$, and the contralateral leg, 2.5 ± 1.0 ml x min^{-1} x $(100\ g)^{-1}$, at rest. During exercise, however, muscle blood flow was significantly ($p < 0.05$) lower in the diseased leg, 29.9 ± 4.8 ml x min^{-1} x $(100\ g)^{-1}$, than in the contralateral leg, 32.4 ± 6.8 ml x min^{-1} x $(100\ g)^{-1}$, Fig. 4. After exercise blood flow decreased to the initial rest value within 5 min in both legs.

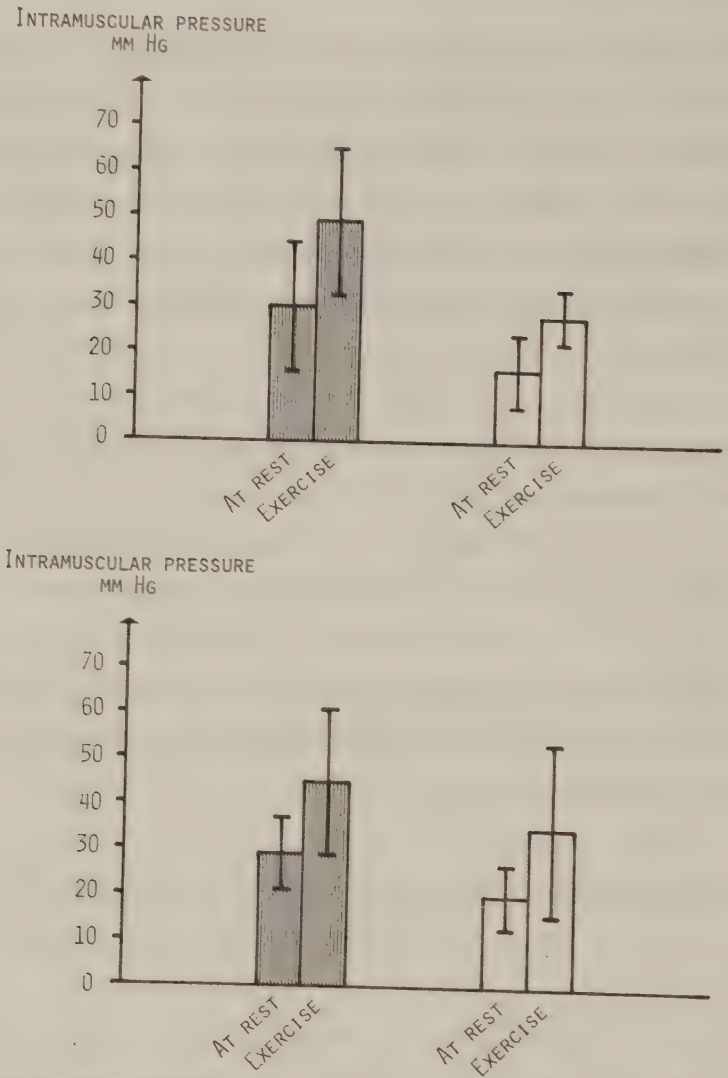

Fig. 2. Intramuscular pressures at rest and during exercise in the anterior tibial (upper diagram) and the deep posterior (lower diagram) compartments of both legs in 7 patients with unilateral lymphedema.

SD is given. ▨ = *lymphedematous leg.*

□ = *control leg.*

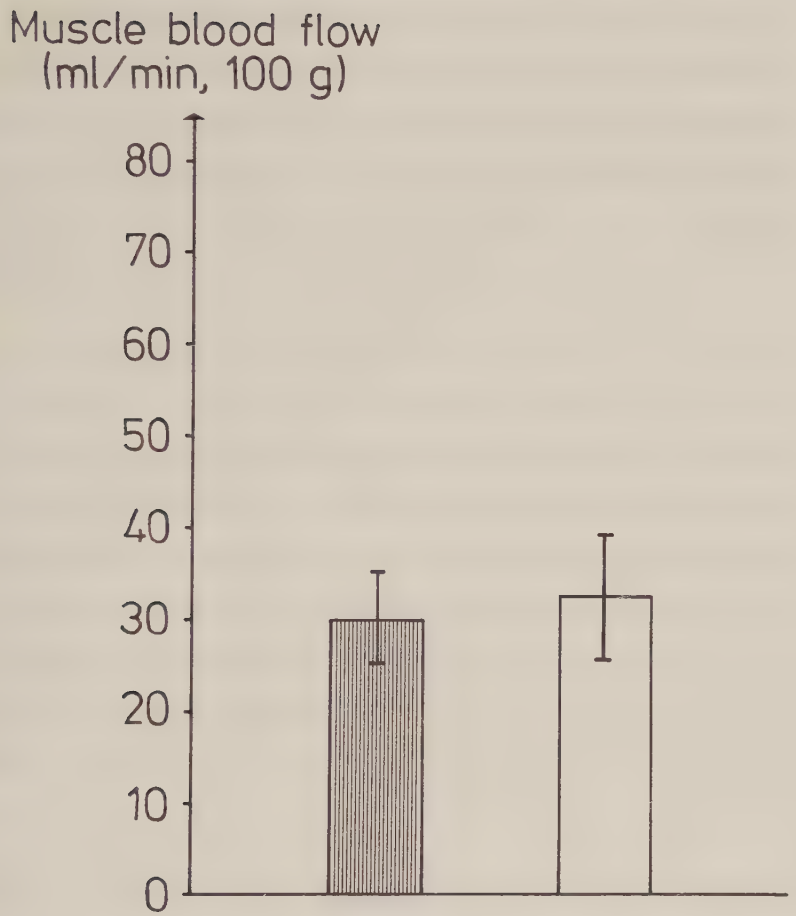

Fig. 3. Muscle blood flow during exercise in both legs of 7 patients with unilateral lymphedema. SD is given. Symbols as in Fig. 2.

Discussion

Lymphatic obstruction leads to an increased tissue concentration of protein giving an increased colloid osmotic pressure in the tissue and resulting in an increased muscle water content (7). An increased muscle water content is known to cause an increased intramuscular pressure (1). In the present study the intramuscular pressure was found to be elevated in both the anterior tibial and the deep posterior compartments of the lymphedematous leg. The increased intramuscular pressure in the present lymphedematous patients may thus be due to an increased interstitial fluid content (1). Venous obstruction in the leg has previously been shown to cause a marked increase in intramuscular pressure (2, 8, 9). The venous function in the present patients was tested by venous emptying. It was significantly lower in the lymphedematous leg than in the contralateral leg although it was subnormal in only two patients out of seven. The reason for the decreased venous emptying may be a partial compression of veins by the increased intramuscular pressure secondary to lymphedema.

Lymphatic obstruction may lead to an increased interstitial (intramuscular) pressure, which may cause a reduced capillary blood flow (7). Many investigators have demonstrated that increased intramuscular pressure reduces muscle blood flow (10, 11, 12). This was also seen in the present study where muscle blood flow during exercise as measured by the clearance of ^{133}Xenon was significantly decreased

in the leg with increased intramuscular pressure due to lymphedema.

It is concluded from the present study that lymphatic obstruction of the leg causes edema which leads to an increased intramuscular pressure. The decreased venous emptying and the decreased muscle blood flow may be due to a compression of the veins and capillaries by the increased intramuscular pressure.

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INTRAMUSCULAR PRESSURE, MUSCLE BLOOD FLOW AND SKELETAL MUSCLE METABOLISM IN THE CHRONIC ANTERIOR TIBIAL COMPARTMENT SYNDROME

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Introduction

The chronic anterior tibial compartment syndrome has been described by Mavor [20] 1956 (one case), French & Price[5] 1962 (two cases), Leach, Hammond & Stryker[16] 1967 (five cases), Kenelly & Blumberg[12] 1962 (two cases), Garfin, Mubarak & Owen[6] 1977 (one case), Puranen & Alavaikko[24] 1981 (ten cases) and Willey, Corall & French[29] 1982 (seven cases). Reneman[26] 1975 has reported the largest series of chronic compartment syndromes (61 cases) and nearly all involved the anterior tibial compartment only. Most cases were young male military personell and the symptoms were bilateral in 95 %. Symptoms of the chronic compartment syndrome are exertion pain similar to that of intermittent claudication although there is no sign of arterial disease. Neurologic symptoms are rare. A fascial defect with muscle hernia is the most specific physical sign of the chronic anterior tibial compartment syndrome[26]. In some cases stiffness and swelling over the affected compartment is seen. The chronic compartment syndrome takes an intermittent course and does not generally lead to destruction within the affected compartments[26]. The intramuscular pressure is always abnormally raised[26].

The pathophysiology of the chronic compartment syndrome is not known. It is provoked by exercise and has also been named exertional compartment syndrome. It has been suggested that arterial[4,7,13] or venous [2,16,23] obstruction are initiating factors. A common concept is that the raised intramuscular pressure causing capillary occlusions is caused by an increase in interstitial fluid[10, 19]. The increased interstitial fluid

is secondary to an increased hyperosmolarity[10,17,28]. The anterior tibial compartment is most commonly affected probably due to its strong fascial covering. Chronic compartment syndromes involving the superficial posterior compartment (gastrocnemius and soleus muscles) are rare [14,21].

There are only few thorough studies of patients with a chronic anterior tibial compartment syndrome. The present study was made in order to 1) demonstrate the intramuscular pressure changes that are diagnostic of a chronic anterior tibial compartment syndrome, 2) evaluate the relationship between muscle blood flow and intramuscular pressure, 3) study the metabolism in the anterior tibial muscles before fasciotomy, 4) test previous arterial and venous occlusion theories in the pathogenesis of this syndrome by determining distal blood pressure and venous emptying and 5) determine the effect of fasciotomy on intramuscular pressure, muscle blood flow and skeletal muscle metabolism.

Material

One hundred and eight nonselected patients with lower leg pain of unknown cause were referred to the Department of Clinical Physiology in the period September 1979 to June 1982 for intramuscular pressure measurement. In 93 patients the intramuscular pressures in the anterior tibial compartment were within normal limits both at rest and during exercise when compared with a reference material[25]. In 15 patients or about 14 % (seven females and eight males, aged 17 - 50, mean 29 years)

the pressures were significantly increased both at rest and during exercise and a bilateral chronic anterior tibial compartment syndrome was diagnosed. These 15 patients were further investigated. The patients' main complaint was pain in the anterior part of the lower leg on exercise. At the moment of pain, active dorsiflexion of the ankle was often difficult. There was no previous history of trauma to the lower leg. On physical examination the patients had bulky, highly developed muscles. Six patients were active runners. Muscle hernias appeared in 6 patients (40 %) and they were more prominent after exercise than at rest. Distal pulses were present in all patients. Neurologic examination was normal. Symptom duration varied from 5 months to 9 (mean 3) years.

Fasciotomy was performed bilaterally in all 15 patients. Following an anterolateral skin incision 5 - 10 cm in length, the anterior tibial and the lateral compartments were decompressed from the fibular head to the lateral malleolus using a Smilley knife.

Methods

Intramuscular pressure measurement. Intramuscular pressure was measured using the wick technique as described in detail previously[25]. The pressures within the anterior tibial and superficial posterior compartments were measured in both legs at rest with the patient in a sitting position. Intramuscular pressures were then measured at maximal workload for 7 min or more if necessary to provoke exertional pain. The exercise consisted of dorsiflexion and plantarflexion of the foot every second. The foot was attached to an isometric exerciser and the workload was

continously monitored only to verify that the work was constant and maximal during the exercise. After exercise the intramuscular pressure was followed until the pressure had returned to the pre-exercise level. The time period for the pressures to reach half way back to the initial resting pressure after exercise (T 1/2) was estimated. Intramuscular pressure measurements were performed bilaterally in the anterior tibial compartment in all 15 patients before and after fasciotomy, and in the superficial posterior compartment before fasciotomy.

Systolic pressure of the big toe was measured with a strain-gauge technique and a standardized walkingtest on the tread mill (speed 1.2 m/sec, inclination 5 %) was carried out to evaluate any arterial disease.

Muscle blood flow was measured in 10 patients in the anterior tibial muscle of the most symptomgiving leg before and after fasciotomy using the ^{133} Xenon clearance technique. Approximately 3.5 MBq ^{133}Xenon in 0.1 ml of isotonic saline was injected into the anterior tibial muscle about 10 cm below the knee joint margin at a depth of about 2 cm using a needle with 0.4 mm outer diameter. The isotope was slowly injected during 15 sec and the needle was withdrawn 15 sec thereafter. Records were taken with the patient at rest in a sitting position, during exercise as described above and during 5 min after exercise. Counting rate was recorded directly over the site of injection with a collimated cadmium telluride detector (TE 101, Pharmacia Electronics, Denmark) attached to the skin surface of the leg with adhesive tape. The detector was connected to a portable memory, Memolog-500 (Pharmacia Electro-

nics, Denmark), working as multiscaler giving digital information of the counting rate variation in 8 sec intervals. The blood flow (f) was calculated from the half-time (T 1/2) of the disappearance of the isotope according to the following formula:

$f = \frac{\ln 2 \cdot \lambda \cdot 60 \cdot 100}{T\ 1/2}$, where λ represents the partition coefficient for ^{133}Xenon between tissue and blood. A standardized value of 0.7 ul/g was used for λ, since it has been used previously for muscle tissue[15]. The calculated muscle blood flow is expressed as ml x min^{-1} x $(100\ g)^{-1}$.

Venous emptying was performed according to Hallböök[8]. A tourniquet applied around the thigh was pumped up to 50 mm Hg. The calf volume was registered with strain gauge technique. When no further increase of calf volume was noted the tourniquet was released and the venous outflow measured. Values below 40 ml x min^{-1} x $(100\ g)^{-1}$ were regarded as subnormal[8].

Metabolic analysis. Muscle biopsies were extracted with Radner forceps (No 13717, AB Stille Werner, Stockholm, Sweden) from the anterior tibial muscle of the most symptomgiving leg in 6 patients before and after fasciotomy about 10 cm beneath the lateral condyle of the tibia under local anesthesia. The biopsies were taken at rest and immediately after a maximal workload for 7 min as described above. The muscle specimens were immediately frozen in isopentane cooled to freezing point and stored at -80°C until analysis. ATP, phosphocreatine (CP) and lactate were analyzed using enzymatic fluorometric techniques. Total muscle

water was obtained by weighing the samples before and after freeze drying.

Results

Intramuscular pressure measurement. In the 15 patients the anterior tibial muscle pressure was 22 (range 18-28) mm Hg at rest rising to 80 (range 48-135) mm Hg during exercise. These pressure values are significantly ($p < 0.001$) higher than the corresponding reference values, 8 (range 2-23) mm Hg and 26 (range 8-60) mm Hg, respectively. The return to resting values took from 10 min to 2 hours (mean 40 min). In two patients there was only a partial return to the resting values in two hours. The time period for the pressures to reach half way back to the initial resting pressure after exercise (T 1/2) was 6 $\pm$ 3 min. T 1/2 is normally 3 $\pm$ 4.0 sec[25].

When studied three months after fasciotomy the pressures were normalized: 14 (range 10-20) mm Hg at rest and 21 (range 11-32) mm Hg during exercise. Furthermore after exercise the pressure was back to the resting level within 1 min (T 1/2 2 $\pm$ 1 sec). In Fig. 1 the pressures after exercise are seen in one patient before and after fasciotomy. In the superficial posterior compartment the pressures were within normal limits[25] at rest, 4 (range 0-15) mm Hg and during exercise 7 (range 1-21) mm Hg. After fasciotomy 14 patients were symptomfree while one patient still had moderate symptoms.

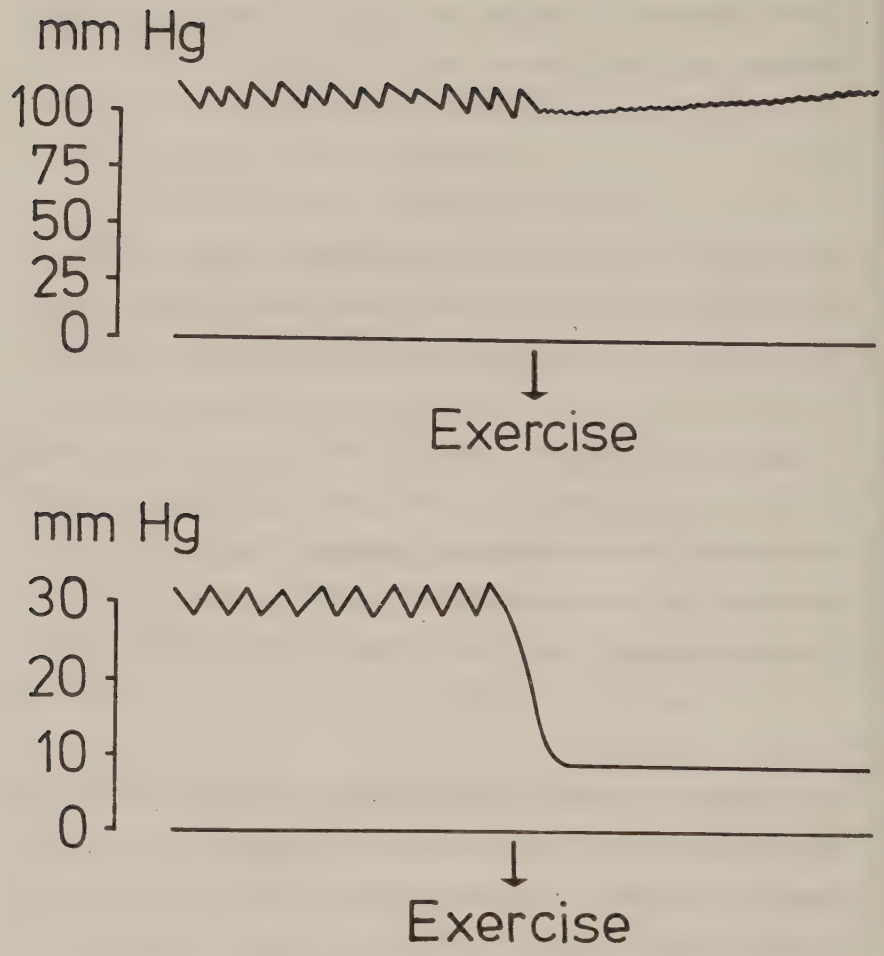

Fig. 1. Anterior tibial compartment pressure curves at the end of exercise in one patient before fasciotomy (a) and after fasciotomy (b).

Systolic pressure of the big toe was normal in all patients. Walking distance was "unlimited" (>1 500 m) in all but 2 patients who stopped after 200 and 536 m, respectively, because of pain in the anterior tibial muscles. Pain in the anterior tibial compartment began after 550 (range 115-1 500) m.

Muscle blood flow at rest was 4.7 ± 2.2 ml x min^{-1} x $(100\ g)^{-1}$, rising to 40.5 ± 3.2 ml x min^{-1} x $(100\ g)^{-1}$ during exercise. After exercise muscle blood flow decreased to preexercise values within 5 min. After fasciotomy the muscle blood flow at rest did not differ significantly to the preoperative rest values, 5.2 ± 2.7 ml x min^{-1} x $(100\ g)^{-1}$. During exercise, on the other hand, muscle blood flow increased to a significantly ($p < 0.001$) higher level after fasciotomy, 54.9 ± 4.3 ml x min^{-1} x $(100\ g)^{-1}$ than before fasciotomy (Fig. 2). After exercise the muscle blood flow returned to the preexercise level within 5 min.

Venous emptying was normal, above 40 ml x min^{-1} x $(100\ g)^{-1}$ in 11 patients, subnormal bilaterally in 2 patients, and unilaterally in 2 patients before fasciotomy. After fasciotomy one patient improved his venous emptying while it was still decreased in three patients. Phlebography was performed in 2 out of these 3 patients and it was found to be normal in both.

Skeletal muscle metabolism. The results are given in Fig, 3. ATP, CP and lactate are expressed in mmol/kg wet weight. The phosphagen stores

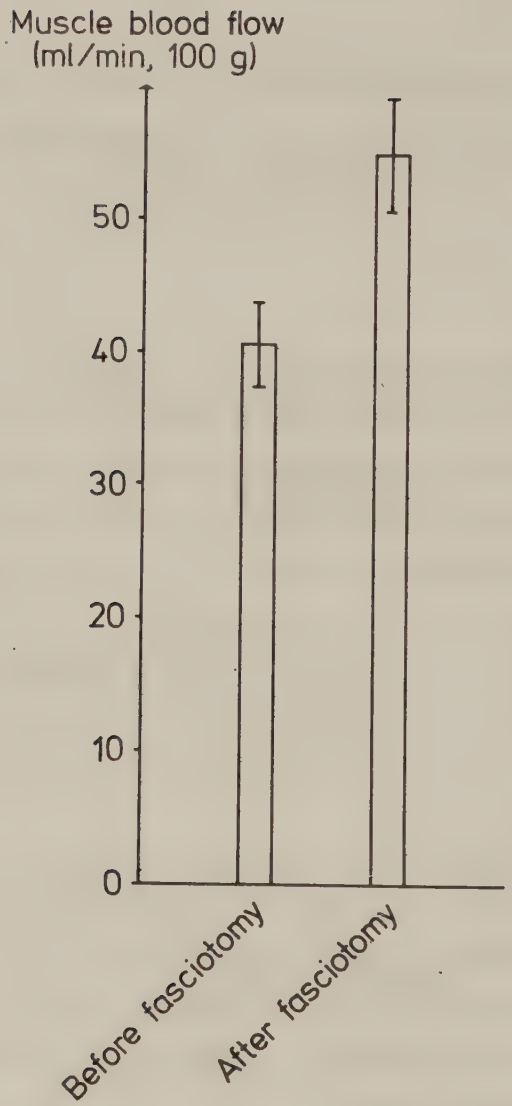

Fig. 2. Muscle blood flow during exercise in 10 patients with a chronic anterior tibial compartment syndrome before and after fasciotomy. SD is given.

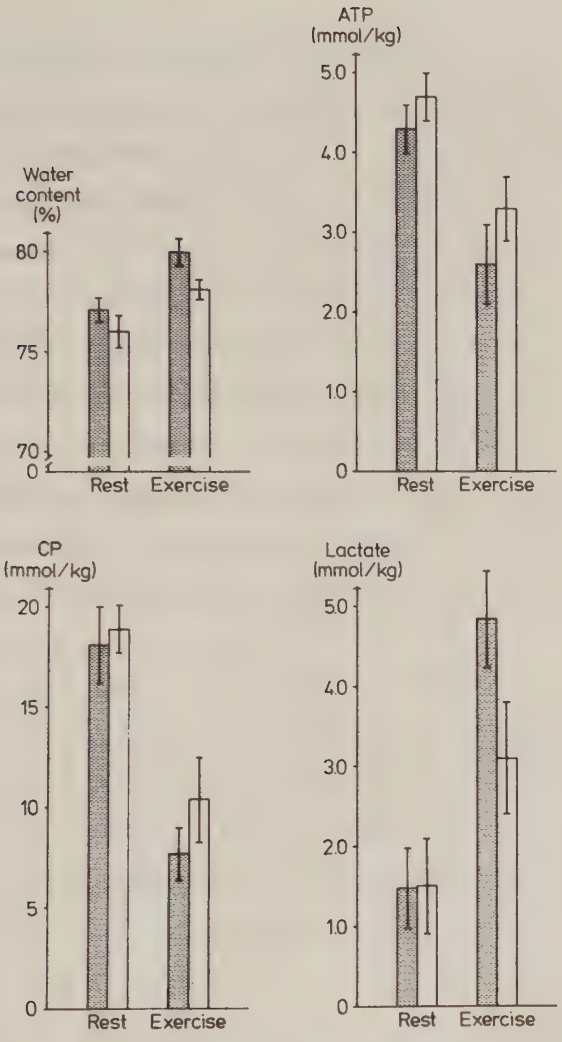

Fig. 3. Muscle water content and concentrations of ATP, CP and lactate in the anterior tibial muscles in 6 patients with a chronic anterior tibial compartment syndrome at rest and immediately after exercise before and after fasciotomy.

▨ *before fasciotomy* ▭ *after fasciotomy*

SD is given.

(ATP, CP) were quite normal at rest both before and after fasciotomy[11]. The exercise caused ATP to become reduced from its resting level of 4:3 ± 0.3 mmol/kg to 2.6 ± 0.5 mmol/kg before fasciotomy and from 4.7 ± 0.3 mmol/kg to 3.3 ± 0.4 mmol/kg after fasciotomy. The reduction of the ATP was significant ($p < 0.001$) both before and after fasciotomy. CP also became reduced with the exercise from 18.1 ± 1.9 mmol/kg to 7.7 ± 1.3 mmol/kg before fasciotomy and from 18.9 ± 1.2 mmol/kg to 10.4 ± 2.1 mmol/kg after fasciotomy ($p < 0.001$). Muscle lactate was normal[11] at rest both before, 1.5 ± 0.5 mmol/kg and after fasciotomy, 1.5 ± 0.6 mmol/kg with a significant increase ($p < 0.01$) with exercise to 4.9 ± 0.6 mmol/kg before fasciotomy and 3.1 ± 0.7 mmol/kg after fasciotomy. The elevation was larger ($p < 0.05$) before fasciotomy.

Muscle water content at rest was slightly higher ($p < 0.05$) 77.1 ± 0.6 % before fasciotomy than after fasciotomy, 76.0 ± 0.6 %. The exercise caused the water content to increase before as well as after fasciotomy. Muscle water content increased to 79.9 ± 0.6 % before and 78.1 ± 0.5 % after fasciotomy. The increase in water content was more pronounced ($p < 0.05$) before than after fasciotomy.

Discussion

The chronic anterior tibial compartment syndrome may be more common than reflected in the literature. In the present series it occurred in 14 % of unselected patients with lower leg pain of unknown cause. The majority of the reported cases are young men which may be due to selected materials. The largest series consisted of military personell[26].

In the present series sex distribution was equal and the mean age was higher than in earlier reports. The amount of exercise sufficient to provoke the symptoms may vary considerably[26]. The walking distance varied in the present series from 200 to over 1 500 m. The symptom duration is usually months to years by the time the diagnosis is made[3, 22]. It was 3 years in our series. Muscle hernias are reported in 20 - 60 % of the cases[22,26]. Forty per cent of the patients in this series had muscle hernias. The presence of muscle hernias may indicate that increased tension within the compartment has existed for a long time. Light manual compression on these hernias prior to exercise resulted in a considerable rise of pressure (unpublished observation). Ischemic necrosis of the muscles in the compartment have occurred following repair of these fascial defects[16,23].

Only a few thorough studies of patients with chronic anterior tibial syndromes have been made. The diagnosis has often been made without intramuscular pressure measurement documentation. Several authors [5,12,24,26] have, however, described an increased intramuscular pressure at rest and after exercise. In the present 15 patients intramuscular pressure was recorded continously at rest as well as during and after exercise with the wick technique. Although the pressures were markedly elevated at rest as well as during exercise compared with normals[25] the most significant finding was an increased pressure return time, 40 min as compared to normally less than one min[25]. The elevated intramuscular pressure in patients with a chronic anterior tibial compartment

syndrome is thought to be due to an increased transudation of fluid during exercise[10,26,28]. This hypothesis is strengthened by the present finding that the water content in the anterior tibial muscle was higher before than after fasciotomy. The anterior tibial compartment has restrictive walls and an increased muscle volume will give an increased intramuscular pressure[22,26]. The intramuscular pressure might remain elevated after exercise until the interstitial fluid volume becomes normal again[26]. The present finding that the pressure return time was as a mean 40 min might indicate that the normalization of muscle water content after exercise is a slow process[18].

It has been reported that if intramuscular pressure exceeds 30 mm Hg the capillary pressure is not sufficient to maintain muscle capillary blood flow[9,10]. Many investigators have demonstrated that increased intramuscular pressure reduces blood flow[1,19,27,28,30]. French & Price[5] and Kenelly & Blumberg[12] found a significantly reduced muscle blood flow as demonstrated by clearance of ^{22}Na-chloride following exercise in 4 patients with a chronic anterior tibial compartment syndrome. A decreased muscle blood flow shown by the clearance of ^{133}Xenon was also found during exercise in the present study.

Metabolic analysis of samples from the anterior tibial muscles before and after fasciotomy revealed a more pronounced elevation of lactate immediately after exercise before fasciotomy. This finding may be explained by the decreased muscle blood flow that was found before fasciotomy and supports the opinion that the exertional pain is

ischemic in its origin[27]. Exercise caused a normal depletion of the ATP and CP concentrations both before and after fasciotomy.

Venous function as estimated with venous emptying and in some cases with phlebography was normal in 87 % of the patients. This finding indicates that venous obstruction is not the major factor for the chronic anterior tibial compartment syndrome.

In conclusion the present study shows that intramuscular pressure is elevated before, during and after exercise in patients with a chronic anterior tibial compartment syndrome. This increment of intramuscular pressure, at least partly due to an increased muscle water content, causes a decreased muscle blood flow and increased muscle lactate levels during exercise. Venous function is normal in the majority of patients. Fasciotomy relieves pain and normalizes intramuscular pressure, muscle blood flow and skeletal muscle metabolism in patients with a chronic anterior tibial compartment syndrome.

Summary

Fifteen cases of a bilateral chronic anterior tibial compartment syndrome were investigated in order to 1) demonstrate the intramuscular pressure changes that are diagnostic of a chronic anterior tibial compartment syndrome, 2) evaluate the relationship between muscle blood flow and intramuscular pressure, 3) study the metabolism in the anterior tibial muscles before fasciotomy, 4) test previous arterial and venous occlusion theories in the pathogenesis of this syndrome by determining distal blood pressure and venous emptying and 5) determine the effect of fasciotomy on intramuscular pressure, muscle blood flow and skeletal muscle metabolism. Intramuscular pressure measured with the wick technique was significantly increased at rest, during and after exercise compared with normals. Muscle blood flow during exercise as measured with the ^{133}Xenon clearance technique was significantly lower before than after fasciotomy. Venous emptying was normal in 11/15 cases. Biopsies from the anterior tibial muscles showed an increased water content and elevated muscle lactate before fasciotomy. The increased intramuscular pressure is at least partly due to the increased muscle water content. This may explain the decreased muscle blood flow and the demonstrated increase in muscle lactate concentration during exercise. Fasciotomy relieved pain and normalized intramuscular pressure, muscle blood flow and skeletal muscle metabolism.

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